מדינת ישראל
STATE OF ISRAEL

Ministry of Justice
Patent Office

משרד המשפטים
לשכת הפטנטים

This is to certify that annexed hereto is a true copy of the documents as originally deposited with the patent application of which particulars are specified on the first page of the annex.

זאת לתעודה כי רצופים בזה העתקים נכונים של המסמכים שהופקדו לכתחילה עם הבקשה לפטנט לפי הפרטים הרשומים בעמוד הראשון של הנספח.

This 19-03-2001 היום

ממונה על הבוחנים
השם הפטנטים

Commissioner of Patents

נתאשר
Certified

חוק הפטנטים, תשכ"ז – 1967
PATENTS LAW, 5727-1967

בקשה לפטנט
Application For Patent

לשימוש הלשכה
For Office Use

מספר: Number	136154
תאריך: Date	16 -05- 2000
הוקדם/נדחה: Ante/Post-dated	

אני, (שם המבקש, מענו ולגבי גוף מאוגד: מקום התאגדותו)
I, (Name and address of applicant, and in case of body corporate-place of incorporation)

קומפיוגן בע"מ, חברה ישראלית מרחוב פנחס רוזן 72, תל אביב 69512, ישראל
Compugen Ltd., Israeli Company of 72, Pinchas Rozen St., Tel Aviv 69512, ISRAEL

בעל אמצאה מכח: הדין — Right of Law — Owner, by virtue of

ששמה הוא
of an invention the title of which is

(בעברית)
(Hebrew)

וריאנטים של גנים המעורבים בסרטן

(באנגלית)
(English)

Variants of tumor involved genes

מבקש בזאת כי ינתן לי עליה פטנט
Hereby apply for a patent to be granted to me in respect thereof.

* בקשת חלוקה Application of Division	* בקשת פטנט מוסף Appl. for Patent of Addition	דרישת דין קדימה* Priority Claim		
מבקשת פטנט from application	* לבקשה/לפטנט to Patent/Appl.	מספר/סימן Number/Mark	תאריך Date	מדינת האיגוד Convention Country
מס' No.	מס' No.			
מיום Dated	מיום Dated			

* יפוי כח: כללי — General
הוגש בעניין — filed in case **P128131**

המען למסירת מסמכים בישראל
Address for Service in Israel

REINHOLD COHN AND PARTNERS
Patent Attorneys
P.O.B. 4060, Tel-Aviv **C. 124544**

חתימת המבקש
Signature of Applicant

For the Applicants,
REINHOLD COHN AND PARTNERS
By : —

This the 15 day of May 2000
היום 15 בחודש May שנת 2000
Year

לשימוש הלשכה
For Office Use

טופס זה כשהוא מוטבע בחותם לשכת הפטנטים ומושלם במספר ובתאריך ההגשה, הנו אישור להגשת הבקשה שפרטיה רשומים לעיל.
This form, impressed with the Seal of the Patent Office and indicating the number and date of filing, certifies the filing of the application the particulars of which are set out above.

* מחק את המיותר
Delete whatever is inapplicable

וריאנטים של גנים המעורבים בסרטן

Variants of tumor involved genes

Compugen Ltd.

קומפיוגן בע"מ

C. 124544

SPLICE VARIANTS OF ONCOGENES

FIELD OF THE INVENTION

The present invention concerns novel nucleic acid sequences, vectors and host cells containing them, amino acid sequences encoded by said sequences, and antibodies reactive with said amino acid sequences, as well as pharmaceutical compositions comprising any of the above. The present invention further concerns methods for screening for candidate activators or deactivators utilizing said amino acid sequences. The invention also concerns diagnostic assays utilizing said sequences.

BACKGROUND OF THE INVENTION

Many genes which are involved with tumors are involved with functions which encourage and promote growth and division of cells. Some tumor-involved cells are expressed only in tumor cells, while others are expressed also in normal cells albeit at lower levels. A specific example of tumor-involved genes are oncogenes, which are muted formed of proto-oncogenes.

Generally, proto-oncogenes code for cellular proteins that relay signals to the cell's nuclei thus stimulating growth. These cellular proteins respond to signals from other cells and the signaling process involves several steps among them binding of growth and proliferation regulating factors to the cell membrane, release of second messenger, and a host of other intermediates, in the cell cytoplasm, and activation in the nucleus of transcription factors which move the cells through their growth cycles.

Proto-oncogenes that code for these various components in the cascade may mutate, thus becoming oncogenes that keep the pathways continuously active regardless of the extracellular signals received by the cell. This may result in over-production of growth factors, flooding of the cell with replication signals, uncontrolled stimulation of the intermediary pathways and unrestrained cell growth driven by elevated levels of transcription factors.

The activation of a proto-oncogene to express its oncogenic potential may occur due to point mutation, chromosome rearrangement, gene amplification (an increase in the number of copies of normal proto-oncogenes within a cell) and viral insertion resulting in the control of the expression of the proto-oncogene by a more active promoter.

Typically, oncogenes exhibit dominant phenotype at the cellular level, i.e. one copy of an activated oncogene is sufficient to produce its oncogenic effect, a phenomena which is termed *"gain of function"*. There is usually a requirement to have more than one mutation in the proto-oncogene in order to change a normal cell line into neoplasia. The oncogene may be transmitted from generation to generation when a proto-oncogene mutates in the germ line, and since as indicated above usually more than one mutation is required, a single mutation results in a dominantly inherited tumor predisposition.

The detection of oncogene is of major importance in the detection of tumors as well as in the detection of predisposition to a specific kind of tumor, which may result from additional mutations on an already mutated pro-oncogene. Oncogenes are detected by a plurality of methods among them PCR amplification, hybridization, as well as detection of the oncogenic product by various immunoassays. The understanding of the site of activity of the oncogene is of course of a major importance in the designing of a suitable therapeutical model for the treatment of the cancer resulting from the activity of said oncogene.

Alternative splicing (AS) is an important regulatory mechanism in higher eukaryotes (P.A. Sharp, *Cell* 77, 805-8152 (1994). It is thought to be one of the most important mechanisms for differential expression related to tissue or development stage specificity. AS influences also: protein stability, protein clearance as well as tissue and cellular localization As may further alter protein function by increasing or decreasing the functionality,and may further affect post translational modifications, It is known to play a major role in numerous biological systems, including human antibody responses, and sex determination in *Drosophila*, (S. Stamm, M.Q. Zhang, T.G. Marr and D.M. Helfman, *Nucleic*

Acids Research **22**, 1515-1526 (1994); B. Chabot, *Trends Genet.* **12**, 472-478 (1996); R.E. Breitbart, A. Andreadis, B. Nadal-Ginard, *Annual Rev. Biochem.*, **56**, 467-495 (1987); C.W. Smith, J.G. Patton, B. Nadal-Ginard, *Annu. Rev. Genet.*, **27**, 527-577 (1989)).

Until recently it was commonly believed that alternative splicing existed in only a small fraction of genes (about 5%). A recent observation based on literature survey of known genes revises this conservative estimate to as high as an estimate that at least 30% of human genes are alternatively spliced (M.S. Gelfand, I. Dubchak, I. Draluk and M. Zorn, *Nucleic Acids Research* **27**, 301-302 (1999). The importance of the actual frequency of this phenomenon lies not only in the direct impact on the number of proteins created (100,000 human genes, for example, would be translated to a much higher number of proteins), but also in the diversity of functionality derived from the process.

Several mechanisms at different stages may be held responsible for the complexity of higher eukaryote which include: alternative splicing at the transcription level, RNA editing at the post-transcriptional level, and post-translational modifications are the ones characterized to date.

GLOSSARY

In the following description and claims use will be made, at times, with a variety of terms, and the meaning of such terms as they should be construed in accordance with the invention is as follows:

"Tumor-involved genes (TIG)" – genes for which there is some scientific indication linking their function, expression, or change in the level of their expressionto tumors. This term does not signify necessarily that the genes cause the tumor (although in some cases this is so) but may also indicate that the genes are a result of the tumor process, for example, they are activated by other genes which are the cause of the tumor.

"Variant nucleic acid sequence" – the sequence shown in any one of SEQ ID NO: 1 to SEQ ID NO: 36, sequences having at least *90% identity* (see below) to said sequence and *fragments* (see below) of the above sequences of least 20 b.p. long. These sequences are sequences coding for a novel, naturally occurring, alternative splice variants of native and known genes which are *tumor-involved genes (TIG)*. It should be emphasized that the novel variants of the present invention are naturally occurring sequences resulting from alternative splicing of the TIGS and not merely truncated, mutated or fragmented forms of known tumor-involved sequences which are artificially produced.

"Variant product – also referred at times as the "variant protein" or ***"variant polypeptide"*** – is an amino acid sequence encoded by the variant nucleic acid sequence which is a naturally occurring mRNA sequence obtained as a result of alternative splicing. The amino acid sequence may be a peptide, a protein, as well as peptides or proteins having *chemically modified* amino acids (see below) such as a glycopeptide or glycoprotein. The variant products are shown in any one of SEQ ID NO: 37 to SEQ ID NO: 72. The term also includes *homologues* (see below) of said sequences in which one or more amino acids has been added, deleted, *substituted* (see below) or *chemically modified* (see below) as well as *fragments* (see below) of this sequence having at least 10 amino acids.

"Nucleic acid sequence" – a sequence composed of DNA nucleotides, RNA nucleotides or a combination of both types and may includes natural nucleotides, chemically modified nucleotides and synthetic nucleotides.

"Amino acid sequence" – a sequence composed of any one of the 20 naturally appearing amino acids, amino acids which have been *chemically modified* (see below), or composed of synthetic amino acids.

"Fragment of variant nucleic acid sequence" – novel short stretch of nucleic acid sequences of at least 20 b.p., which does not appear as a continuous stretch in the *original nucleic acid sequence* (see below). The fragment may be a sequence which was previously undescribed in the context of the published RNA and which affects the amino acid sequence encoded by the known oncogene. For example, where the variant nucleic includes a sequence which was not included in the original sequence of the oncogene (for example a sequence which was an intron in the original sequence) the fragment may contain said additional sequence. The fragment may also be a region which is not an intron, which was not present in the original sequence of the TIG. For example where the variant lacks a non-terminal region which was present in the original sequence of the TIG. The two stretches of nucleotides spanning this region (upstream and downstream) are brought together by splicing in the variant, but are spaced from each by the spliced out region in the original sequence of the TIG and are thus not continuous in the original sequence. A continuous stretch of nucleic acids comprising said two sparing stretches of nucleotides is not present in the original sequence of the TIG and thus falls under the definition of fragment.

"Fragments of variant products" - novel amino acid sequences coded by the *"fragment of variant nucleic acid sequence"* defined above.

"Homologues of variants" – amino acid sequences of variants in which one or more amino acids has been added, deleted or replaced. The addition, deletion or replacement should be in the regions or adjacent to regions where the variant differs from the *original sequence* (see below) of the TIG.

"Conservative substitution" - refers to the substitution of an amino acid in one class by an amino acid of the same class, where a class is defined by common physicochemical amino acid side chain properties and high substitution frequencies in homologous proteins found in nature, as determined, for example,

by a standard Dayhoff frequency exchange matrix or BLOSUM matrix. [Six general classes of amino acid side chains have been categorized and include: Class I (Cys); Class II (Ser, Thr, Pro, Ala, Gly); Class III (Asn, Asp, Gln, Glu); Class IV (His, Arg, Lys); Class V (Ile, Leu, Val, Met); and Class VI (Phe, Tyr, Trp). For example, substitution of an Asp for another class III residue such as Asn, Gln, or Glu, is a conservative substitution.

"Non-conservative substitution" - refers to the substitution of an amino acid in one class with an amino acid from another class; for example, substitution of an Ala, a class II residue, with a class III residue such as Asp, Asn, Glu, or Gln.

"Chemically modified" - when referring to the product of the invention, means a product (protein) where at least one of its amino acid resides is modified either by natural processes, such as processing or other post-translational modifications, or by chemical modification techniques which are well known in the art. Among the numerous known modifications typical, but not exclusive examples include: acetylation, acylation, amidation, ADP-ribosylation, glycosylation, GPI anchor formation, covalent attachment of a lipid or lipid derivative, methylation, myristlyation, pegylation, prenylation, phosphorylation, ubiqutination, or any similar process.

"Biologically active" - refers to the variant product having some sort of biological activity, for example, some physiologically measurable effect on target cells, molecules or tissues.

"Immunologically active" defines the capability of a natural, recombinant or synthetic varient product, or any fragment thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies. Thus, for example, an immunologically active fragment of variant product denotes a fragment which retains some or all of the immunological properties of

the variant product, e.g can bind specific anti-variant product antibodies or which can elicit an immune response which will generate such antibodies or cause proliferation of specific immune cells which produce variant.

"Optimal alignment" - is defined as an alignment giving the highest percent identity score. Such alignment can be performed using a variety of commercially available sequence analysis programs, such as the local alignment program LALIGN using a ktup of 1, default parameters and the default PAM. A preferred alignment is the one performed using the CLUSTAL-W program from MacVector (TM), operated with an open gap penalty of 10.0, an extended gap penalty of 0.1, and a BLOSUM similarity matrix. If a gap needs to be inserted into a first sequence to optimally align it with a second sequence, the percent identity is calculated using only the residues that are paired with a corresponding amino acid residue (i.e., the calculation does not consider residues in the second sequences that are in the *"gap"* of the first sequence). In case of alignments of known gene sequences with that of the new variant, the optimal alignment invariably included aligning the identical parts of both sequences together, then keeping apart and unaligned the sections of the sequences that differ one from the other.

"Having at least 90% identity" - with respect to two amino acid or nucleic acid sequences, refers to the percentage of residues that are identical in the two sequences when the sequences are optimally aligned. Thus, 90% amino acid sequence identity means that 90% of the amino acids in two or more optimally aligned polypeptide sequences are identical, however this definition explicitly excludes sequences which are 100% identical with the original sequence from which the variant of the invention was varied.

"Isolated nucleic acid molecule having an variant nucleic acid sequence" - is a nucleic acid molecule that includes the coding variant nucleic acid sequence. Said

isolated nucleic acid molecule may include the variant nucleic acid sequence as an independent insert; may include the variant nucleic acid sequence fused to an additional coding sequences, encoding together a fusion protein in which the variant coding sequence is the dominant coding sequence (for example, the additional coding sequence may code for a signal peptide); the variant nucleic acid sequence may be in combination with non-coding sequences, e.g., introns or control elements, such as promoter and terminator elements or 5' and/or 3' untranslated regions, effective for expression of the coding sequence in a suitable host; or may be a vector in which the variant protein coding sequence is a heterologous.

"Expression vector" - refers to vectors that have the ability to incorporate and express heterologous DNA fragments in a foreign cell. Many prokaryotic and eukaryotic expression vectors are known and/or commercially available. Selection of appropriate expression vectors is within the knowledge of those having skill in the art.

"Deletion" - is a change in either nucleotide or amino acid sequence in which one or more nucleotides or amino acid residues, respectively, are absent.

"Insertion" or "addition" - is that change in a nucleotide or amino acid sequence which has resulted in the addition of one or more nucleotides or amino acid residues, respectively, as compared to the naturally occurring sequence.

"Substitution" - replacement of one or more nucleotides or amino acids by different nucleotides or amino acids, respectively. As regards amino acid sequences the substitution may be conservative or non- conservative.

"Antibody" – refers to IgG, IgM, IgD, IgA, or IgG antibody. The definition includes polyclonal antibodies or monoclonal antibodies. This term refers to

whole antibodies or fragments of the antibodies comprising the antigen-binding domain of the anti-variant product antibodies, e.g. antibodies without the Fc portion, single chain antibodies, fragments consisting of essentially only the variable, antigen-binding domain of the antibody, etc.

Distinguishing antibody" – an antibody capable of binding to the variant product and not the original amino acid sequence of the tumor-involved gene from which it has been varied, or an antibody capable of binding to the original nucleic acid sequence and not to the variant product.

"Activator" - as used herein, refers to a molecule which mimics the effect of the natural variant product or at times even increases or prolongs the duration of the biological activity of said product, as compared to that induced by the variant product. The mechanism may be by any mechanism known to prolonging activities of biological molecules such as binding to receptors; prolonging the lifetime of the molecules; increasing the activity of the molecules on its target; increasing the affinity of molecules to its receptor; inhibiting degradation or proteolysis of the molecules, or mimicking the biological activity of the variants on their targets, etc. Activators may be polypeptides, nucleic acids, carbohydrates, lipids, or derivatives thereof, or any other molecules which can bind to and activate the variant product.

"Deactivator" or ***("Inhibitor")*** - refers to a molecule which modulates the activity of the variant product in an opposite manner to that of the activator, by decreasing or shortening the duration of the biological activity of the variant product. This may be done by any mechanism known to deactivate or inhibit biological molecules such as block of the receptor, block of active site, competition on binding site in target, enhancement of degradation, etc. Deactivators may be polypeptides, nucleic acids, carbohydrates, lipids, or

derivatives thereof, or any other molecules which bind to and modulate the activity of said product.

"Treating a disease" - refers to administering a therapeutic substance effective to ameliorate symptoms associated with a disease, to lessen the severity or cure the disease, or to prevent the disease from occurring. Typically the disease is cancer.

"***Detection***" – refers to a method of detection of a cancer. This term may refer to detection of a predisposition to cancer as well as for establishing the prognosis of the patient by determining the severity of the disease, i.e. determining in which stage the cancer is.

"Probe" – the variant nucleic acid sequence, or a sequence complementary therewith, when used to detect presence of other similar sequences in a sample. The detection is carried out by identification of hybridization complexes between the probe and the assayed sequence. The probe may be attached to a solid support or to a detectable label.

"Original sequence" – the amino acid or nucleic acid sequence of the tumor-involved gene (TIG) from which the variant of the invention have been varied as a result of alternative slicing. This sequence will also be referred to at times as *"tumor-involved-gene" (TIG)*.

SUMMARY OF THE INVENTION

The present invention is based on the finding of several novel, naturally occurring splice variants, which are naturally occurring sequences obtained by alternative splicing of known genes which expression was reported in scientific literature to be involved with tumors (hereinafter *"tumor-involved genes"* or *"TIGS"*). The above term does not signify that the gene necessarily caused the

tumor (although this may be so), merely that they are involved therewith (i.e. expressed in tumors) and this expression may be the result of other effects, for example, as a result of expression of other genes. The novel splice variants of the invention are not merely truncated forms, fragments or mutations of the known tumor-involved genes, but rather novel sequences which naturally occur within the body of individuals, and thus have physiological significance.

The term *"alternative splicing"* in the context of the present invention and claims refers to: intron inclusion, exon exclusion, addition or deletion of terminal sequences in the variant as compared to the original sequences, as well as to the possibility of *"intron retention"*. Intron retention is an intermediate stage in the processing of RNA transcripts, where prior to production of fully processed mRNA the intron (naturally spliced in the original TIG sequence) is retained in the variant. These intermediately processed RNAs may have physiological significance and are also within the scope of the invention.

The novel variant products of the invention may have the same physiological activity as the original tumor-involved peptide from which they have been varied (although perhaps at a different level); may have an opposite physiological activity from the activity featured by the original tumor-involved peptide from which they are varied; may have a completely different, unrelated activity to the activity of the original tumor-involved peptide which they are varied; or alternatively may have no activity at all and this may lead to various diseases or pathological conditions, especially cancer. Both in the case the variant has the same activity as well as the case it has the opposite activity as the original TIG sequence, it may differ from the TIG in its stability, its clearance rate and rate of degradation its tissue and cellular localization, its ligand specificity, its cellular distribution, its temporal expression pathway, manner for up and down regulation and in other biological properties not necessarily connected to activity.

The novel variants may also serve for detection purposes, i.e. their presence or level may be cancer, a predisposition to cancer or the stage and aggression of the cancer disease, or alternatively the ratio between the level variants and the level

original peptide from which they were varied, or the ratio to other variants (all obtained by alternative splicing from the same original sequence of the tumor-involved gene) may be indicative of the presence of cancer, predisposition to cancer or the stage and aggressiveness of the cancer disease.

For example, for detectional purposes, it is possible to establish differential expression of various variants in various tissues. A certain variant may be expressed mainly in one tissue, while the original sequence (tumor-involved sequence) from which it has been varied, or another variant (obtained by alternative splicing from the same original tumor-involved sequence) may, be expressed mainly in another tissue. Understanding of the distribution of the variants in various tissues may be helpful in basic research, for understanding the physiological function of the original tumor-involved genes from which they have been varied, as well as help in targeting pharmaceuticals or in developing pharmaceuticals, and in establishing more accurate modalities of diagnosis.

The study of the variants may also be helpful in distinguishing various stages in the life cycles of the same type of cells which may also be helpful for development of pharmaceuticals for various cancer stages in which cell cycles is non-normal.

Thus the detection may by determination of the presence or the level of expression of the variant within a specific cell population, comparing said presence or level between various cell types in a tissue, between different tissues and between individuals.

Thus the present invention provides by its first aspect, a novel isolated nucleic acid molecule comprising or consisting of any one of the coding sequence SEQ ID NO: 1 to SEQ ID NO: 36, fragments of said coding sequence having at least 20 nucleic acids (provided that said fragments are continuous stretches of nucleotides not present in the original sequence from which the variant was varied), or a molecule comprising a sequence having at least 90%, identity to SEQ ID NO: 1 to SEQ ID NO: 36, provided that the molecule is not completely identical to

the original sequence of the tumor-involved gene from which the variant was varied.

The present invention further provides a protein or polypeptide comprising or consisting of an amino acid sequence encoded by any of the above nucleic acid sequences, termed herein *"variant product"*, for example, an amino acid sequence having the sequence as depicted in any one of SEQ ID NO: 37 to SEQ ID NO: 72, fragments of the above amino acid sequence having a length of at least 10 amino acids coded by the above fragments of the nucleic acid sequences, as well as homologues of the above amino acid sequences in which one or more of the amino acid residues has been substituted (by conservative or non-conservative substitution) added, deleted, or chemically modified.

The deletions, insertions and modifications should be in regions, or adjacent to regions, wherein the variant differs from the original sequence of the tumor-involved gene.

For example, where the variant is different from the original sequence of the tumor-involved gene by addition of a short stretch of 10 amino acids, in the terminal or non- terminal portion of the peptide i.e. inclusion of an exon, the invention also concerns homologues of that variant where the additional short stretch is altered for example, it includes only 8 additional amino acids, includes 13 additional amino acids, or it includes 10 additional amino acids, however some of them being conservative or non-conservative substitutes of the original additional 10 amino acids of the novel variants. In all cases the changes in the homolog, as compared to the original tumor-involved sequence, are in the same regions where the variant differs from the original sequence, or in regions adjacent to said region.

Another example is where the variant lacks a non-terminal region (for example of 20 amino acids) which is present in the original tumor-involved sequence (due for example to exon exclusion). The homologues may lack in the same region only 17 amino acids or 23 amino acids. Again the deletion is in the same region where the variant lacks a sequence as compared to the original tumor-involved sequence, or in a region adjacent thereto. It should be appreciated

that once a man versed in the art's attention is directed to the importance of a specific region, due to the fact that this region differs in the variant as compared to the original sequence of the tumor-involved gene, there is no problem in derivating said specific region by addition to it, deleting from it, or substituting some amino acids in it. Thus homologues of variants which are derivated from the variant by changes (deletion, addition, substitution) only in said region as well as in regions adjacent to it are also a part of the present invention. Generally, if the variant is distinguished from the original sequence of the tumor-involved gene by some sort of physiological activity, then the homolog is distinguished from the original tumor-involved sequence in essentially the same manner.

The present invention further provides nucleic acid molecule comprising or consisting of a sequence which encodes the above amino acid sequences, (including the fragments and homologues of the amino acid sequences). Due to the degenerative nature of the genetic code, a plurality of alternative nucleic acid sequences, beyond those depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 36, can code for the amino acid sequences of the invention. Those alternative nucleic acid sequences which code for the same amino acid sequences as coded by the sequence SEQ ID NO: 1 to SEQ ID NO: 36 (i.e. SEQ ID NO: 37 to SEQ ID NO: 72) are also an aspect of the of the present invention.

The present invention further provides expression vectors and cloning vectors comprising any of the above nucleic acid sequences, as well as host cells transfected by said vectors.

The present invention still further provides pharmaceutical compositions comprising, as an active ingredient, said nucleic acid molecules, said expression vectors, or said protein or polypeptide.

These pharmaceutical compositions are suitable for the treatment of various cancers, which can be ameliorated or cured by raising the level of any one of the variant products of the invention.

By a second aspect, the present invention provides a nucleic acid molecule comprising or consisting of a non-coding sequence which is complementary to that

of any one of SEQ ID NO: 1 to SEQ ID NO: 36, or complementary to a sequence having at least 90% identity to said sequence (with the proviso added above) or a fragment of said two sequences (according to the above definition of fragment). The complementary sequence may be a DNA sequence which hybridizes with any one of SEQ of ID NO: 1 to SEQ ID NO: 36 or hybridizes to a portion of that sequence having a length sufficient to inhibit the transcription of the complementary sequence. The complementary sequence may be a DNA sequence which can be transcribed into an mRNA being an antisense to the mRNA transcribed from any one of SEQ ID NO: 1 to SEQ ID NO: 36 or into an mRNA which is an antisense to a fragment of the mRNA transcribed from any one of SEQ ID NO: 1 to SEQ ID NO: 36 which has a length sufficient to hybridize with the mRNA transcribed from SEQ ID NO: 1 to SEQ ID NO: 36, so as to inhibit its translation. The complementary sequence may also be the mRNA or the fragment of the mRNA itself.

The nucleic acids of the second aspect of the invention may be used for therapeutic or diagnostic applications for example as probes used for the detection of the variants of the invention. The presence of the variant transcript or the level of the variant transcript may be indicative of cancer, predisposition to cancer or the stage or aggressiveness of the cancer disease. In addition or alternatively, the ratio of the level of the transcripts of the variants of the invention may also be compared to that of the transcripts of the original sequences of the oncogenes from which have been varied, or to the level of transcript of other variants (especially obtained by alternative splicing from the same original sequence), and said ratio may be indicative of cancer, predisposition to cancer or the stage or aggressiveness of the cancer disease

The present invention also provides expression vectors comprising any one of the above defined complementary nucleic acid sequences and host cells transfected with said nucleic acid sequences or vectors, being complementary to those specified in the first aspect of the invention.

The invention also provides anti-variant product antibodies, namely antibodies directed against the variant product which specifically bind to said variant product. Said antibodies are useful both for diagnostic and therapeutic purposes. For example said antibody may be as an active ingredient in a pharmaceutical composition as will be explained below.

The present invention also provides pharmaceutical compositions comprising, as an active ingredient, the nucleic acid molecules which comprise or consist of said complementary sequences, or of a vector comprising said complementary sequences. The pharmaceutical composition thus provides pharmaceutical compositions comprising, as an active ingredient, said anti-variant product antibodies.

The pharmaceutical compositions comprising said anti-variant product antibodies or the nucleic acid molecule comprising said complementary sequence, are suitable for the treatment of diseases and pathological conditions where a therapeutically beneficial effect may be achieved by neutralizing the variant (either at the transcript or product level) or decreasing the amount of the variant product or blocking its binding to its target, for example, by the neutralizing effect of the antibodies, or by the effect of the antisense mRNA in decreasing the expression level of the variant sequence. In particular these diseases are cancer diseases and the treatment may also be for amelioration of cancer or for prevention of cancer purposes.

According to the third aspect of the invention the present invention provides methods for detecting the level of the transcript (mRNA) of said variant product in a body fluid sample, or in a specific tissue sample, for example by use of probes comprising or consisting of said coding sequences; as well as methods for detecting levels of expression of said product in tissue, e.g. by the use of antibodies capable of specifically reacting with the variant products of the invention. Detection of the level of the expression of the variant of the invention in particular as compared to that of the original tumor-involved gene sequence from which it was varied or compared to other variant sequences all varied from the same original TIG

sequence may be indicative of a cancer, predisposition to cancer or the stage or aggressiveness of the cancer disease

The method, according to this latter aspect, for detection of a nucleic acid sequence which encodes the variant product in a biological sample, comprises the steps of:

(a) providing a probe comprising at least one of the nucleic acid sequences defined above;

(b) contacting the biological sample with said probe under conditions allowing hybridization of nucleic acid sequences thereby enabling formation of hybridization complexes;

(c) detecting hybridization complexes, wherein the presence of the complexes indicates the presence of nucleic acid sequence encoding the variant product in the biological sample.

The method as described above is qualitative, i.e. indicates whether the transcript is present in or absent from the sample. The method can also be quantitative, by determining the level of hybridization complexes and then calibrating said levels to determining levels of transcripts of the desired variant in the sample.

Both qualitative and quantitative determination methods can be used for diagnostic, prognostic and therapy planning purposes, especially in conjunction with cancer diseases. In addition qualitative determination may be indicative of the cancer stage.

By a preferred embodiment the probe is part of a nucleic acid chip used for detection purposes, i.e. the probe is a part of an array of probes each present in a known location on a solid support.

The nucleic acid sequence used in the above method may be a DNA sequence an RNA sequence, etc; it may be a coding or a sequence or a sequence complementary thereto (for respective detection of RNA transcripts or coding-DNA sequences). By quantization of the level of hybridization complexes

and calibrating the quantified results it is possible also to detect the level of the transcript in the sample.

Methods for detecting mutations in the region coding for the variant product are also provided, which may be methods carried-out in a binary fashion, namely merely detecting whether there is any mismatches between the normal variant nucleic acid sequence of the invention and the one present in the sample, or carried-out by specifically detecting the nature and location of the mutation. Detection of mutations may be of importance in the determination of predisposition to cancer, as well as in attempts to establish the prognosis of the cancer disease.

The present invention also concerns a method for detecting variant product in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of the invention, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of variant product in said biological sample.

Many diseases are diagnosed by detecting the presence of antibodies against a protein characterizing the disease in the blood, serum or any other body fluid of the patient. The present invention also concerns a method for detecting anti-variant antibody in a biological sample, comprising:

(a) contacting said sample with the variant product of the invention, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of anti-variant antibody in the sample.

As indicated above, both methods (for detection of variant product and for detection of the anti-variant antibody) can be quantitized to determine the level or the amount of the variant or antibody in the sample, alone or in comparison to the level of the original amino acid tumor-involved sequence from which it was varied or compared to the level of antibodies against the original amino acid sequence,

and qualitative and quantitative results may be used for diagnostic, prognostic and therapy planning purposes.

The invention also concerns distinguishing antibodies, i.e. antibodies capable of binding either to the variant product or to the original tumor-involved gene sequence from which the variant has been varied, while not binding to the original sequence or the variant product respectively. These distinguishing antibodies may be used for detection purposes.

By yet another aspect the invention also provides a method for identifying candidate compounds capable of binding to the variant product and modulating its activity (being either activators or deactivators). The method includes:

(i) providing a protein or polypeptide comprising an amino acid sequence substantially as depicted in any one of SEQ ID NO: 37 to 72, or a fragment of such a sequence;

(ii) contacting a candidate compound with said amino acid sequence;

(iii) measuring the physiological effect of said candidate compound on the activity of the amino acid sequences and selecting those compounds which show a significant effect on said physiological activity.

The present invention also concerns compounds identified by the above methods described above, which compound may either be an activator of the variant product or a deactivator thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be carried out in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which:

Fig. 1 is a comparison between the amino acid sequence of SEQ ID NO: 37 and the original tumor-involved sequence from which it has been varied;

Fig. 2 is a comparison between the amino acid sequence of SEQ ID NO: 38 and the original tumor-involved sequence from which it has been varied;

Fig. 3 is a comparison between the amino acid sequence of SEQ ID NO: 39 and the original tumor-involved sequence from which it has been varied;

Fig. 4 is a comparison between the amino acid sequence of SEQ ID NO: 40 and the original tumor-involved sequence from which it has been varied;

Fig. 5 is a comparison between the amino acid sequence of SEQ ID NO: 41 and the original tumor-involved sequence from which it has been varied;

Fig. 6 is a comparison between the amino acid sequence of SEQ ID NO: 42 and the original tumor-involved sequence from which it has been varied;

Fig. 7 is a comparison between the amino acid sequence of SEQ ID NO: 43 and the original tumor-involved sequence from which it has been varied;

Fig. 8 is a comparison between the amino acid sequence of SEQ ID NO: 44 and the original tumor-involved sequence from which it has been varied;

Fig. 9 is a comparison between the amino acid sequence of SEQ ID NO: 45 and the original tumor-involved sequence from which it has been varied;

Fig. 10 is a comparison between the amino acid sequence of SEQ ID NO: 46 and the original tumor-involved sequence from which it has been varied;

Fig. 11 is a comparison between the amino acid sequence of SEQ ID NO: 47 and the original tumor-involved sequence from which it has been varied;

Fig. 12 is a comparison between the amino acid sequence of SEQ ID NO: 48 and the original tumor-involved sequence from which it has been varied;

Fig. 13 is a comparison between the amino acid sequence of SEQ ID NO: 49 and the original tumor-involved sequence from which it has been varied;

Fig. 14 is a comparison between the amino acid sequence of SEQ ID NO: 50 and the original tumor-involved sequence from which it has been varied;

Fig. 15 is a comparison between the amino acid sequence of SEQ ID NO: 51 and the original tumor-involved sequence from which it has been varied;

Fig. 16 is a comparison between the amino acid sequence of SEQ ID NO: 52 and the original tumor-involved sequence from which it has been varied;

Fig. 17 is a comparison between the amino acid sequence of SEQ ID NO: 53 and the original tumor-involved sequence from which it has been varied;

Fig. 18 is a comparison between the amino acid sequence of SEQ ID NO: 54 and the original tumor-involved sequence from which it has been varied;

Fig. 19 is a comparison between the amino acid sequence of SEQ ID NO: 55 and the original tumor-involved sequence from which it has been varied;

Fig. 20 is a comparison between the amino acid sequence of SEQ ID NO: 56 and the original tumor-involved sequence from which it has been varied;

Fig. 21 is a comparison between the amino acid sequence of SEQ ID NO: 57 and the original tumor-involved sequence from which it has been varied;

Fig. 22 is a comparison between the amino acid sequence of SEQ ID NO: 58 and the original tumor-involved sequence from which it has been varied;

Fig. 23 is a comparison between the amino acid sequence of SEQ ID NO: 59 and the original tumor-involved sequence from which it has been varied;

Fig. 24 is a comparison between the amino acid sequence of SEQ ID NO: 60 and the original tumor-involved sequence from which it has been varied;

Fig. 25 is a comparison between the amino acid sequence of SEQ ID NO: 61 and the original tumor-involved sequence from which it has been varied;

Fig. 26 is a comparison between the amino acid sequence of SEQ ID NO: 62 and the original tumor-involved sequence from which it has been varied;

Fig. 27 is a comparison between the amino acid sequence of SEQ ID NO: 63 and the original tumor-involved sequence from which it has been varied;

Fig. 28 is a comparison between the amino acid sequence of SEQ ID NO: 64 and the original tumor-involved sequence from which it has been varied;

Fig. 29 is a comparison between the amino acid sequence of SEQ ID NO: 65 and the original tumor-involved sequence from which it has been varied;

Fig. 30 is a comparison between the amino acid sequence of SEQ ID NO: 66 and the original tumor-involved sequence from which it has been varied;

Fig. 31 is a comparison between the amino acid sequence of SEQ ID NO: 67 and the original tumor-involved sequence from which it has been varied;

Fig. 32 is a comparison between the amino acid sequence of SEQ ID NO: 68 and the original tumor-involved sequence from which it has been varied;

Fig. 33 is a comparison between the amino acid sequence of SEQ ID NO: 69 and the original tumor-involved sequence from which it has been varied;

Fig. 34 is a comparison between the amino acid sequence of SEQ ID NO: 70 and the original tumor-involved sequence from which it has been varied;

Fig. 35 is a comparison between the amino acid sequence of SEQ ID NO: 71 and the original tumor-involved sequence from which it has been varied;

Fig. 36 is a comparison between the amino acid sequence of SEQ ID NO: 72 and the original tumor-involved sequence from which it has been varied.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Example I: Comparison of variants with original sequences

Original sequences of tumor-involved genes were obtained from GenBank Version 115. Their tumor involvement was determined by comparison between the original sequences and the noval variant sequences was made using the BestFit application from the GCG suite version 10.0 (January 1999), with the defalut values:

Gap creation penalty (GapWeight): 50

Gap extension penalty (GapLengthWeight): 3

The comparison is shown in Fig. 1 to 34 which show the comparison of each of the variant products depicted in SEQ ID NO: 37 to 72 with the original tumor-involved sequence from which it was varied.

The following is a list which gives the name and the description of each original tumor-involved sequence from which the alternative splice variant has been varied by alternative splicing. The description is followed by the internal reference to the novel variant (NV-... etc.) and a short comparison between the variant and the original tumor-involved sequence. It should be noticed that several splice variants may have been originated from the same parent sequence by several different alternative splicings. The following table summarizes the accession number of the original sequence, the terminology of the new variant (NV-1 to

NV-34) and the description of the difference between the new variant and the original sequence.

Table

Accession	New variant #	Description of the new variant
KU70_HUMAN	NV-1	The new variant has an alternative 3' exon of 5 aa instead of 240 amino acids. It is probably missing the PHOSPHORYLATION (BY NUCLEAR KINASE NII) site and half of the PRO-RICH domain but retains the LEUCINE-ZIPPER domain.
KU70_HUMAN	NV-2	The new variant has a deletion of 210 aa between residues 304 – 515. Lacks the Pro-rich domain but retains the LEUCINE-ZIPPER domain and PHOSPHORYLATION (BY NUCLEAR KINASE NII) site.
LCK_HUMAN	NV-3	The new variant has an alternative 3' exon of 45 amino acids instead of 163 amino acids. The new variant retains both SH domains and most of the PROTEIN KINASE domain including two ATP BINDING sites and the ACTIVE SITE. It is missing the 3' end of the PROTEIN KINASE domain and lacks the AUTO-PHOSPHORYLATION and PHOSPHORYLATION sites.
LCK_HUMAN	NV-4	Insertion of 58 amino acids after amino acid 62 (insertion does not result in truncation). Insertion in first SH2 domain. The new variant retains all important sites including: the PROTEIN KINASE DOMAIN with two ATP BINDING sites, an ACTIVE SITE and an AUTO PHOSPHORYLATION site. An additional PHOSPHORYLATION site.

OSTP_HUMAN	NV-5	The new variant has an alternative 3' exon of 12 aa instead of 134 aa. The new variant maintains the CELL ATTACHMENT SITE and two GLYCOSILATION sites.
GA45_HUMAN	NV-6	The new variant has an alternative 5' exon of 72 amino acids instead of 125 amino acids. The new variant has a signal peptide and has the two PHOSPHORYLATION (BY CK2) sites.
WN11_HUMAN	NV-7	The new variant has a deletion of 22 amino acids after residue 312 (between 312-334). The new variant has all five potential GLYCOSILATION sites.
WN11_HUMAN	NV-8	The new variant has a deletion of 117 amino acids after residue 116 (between 116-233). The new variant is missing one potential GLYCOSILATION site (out of 5 sites).
KPCT_HUMAN	NV-9	The new variant has an alternative 3' exon of 3 amino acids instead of 94 amino acids. The alternative region is in the protein kinase domain. The new variant maintains the two PHORBOL-ESTER AND DAG BINDING domains, the two ATP binding sites and the active site of the kinase domain.
IRF1_HUMAN	NV-10	The new variant has an alternative 3' exon of 7 amino acids instead of 40 amino acids. The new variant maintains the DNA binding domain.
FGR1_HUMAN	NV-11	The new variant has an alternative 3' exon of 14 amino acids instead of 134 amino acids. The new variant has the entire extracellular domain and the TM, it is missing part of the cytoplasmic domain. The new variant

		maintains all 3 IMMUNO-GLOBULIN-LIKE DOMAINS, the protein KINASE domain, the ACTIVE site, and the 2 ATP binding sites, but it might be missing one of the two PHOSPHORYLATION (AUTO-) sites.
APE1_HUMAN	NV-12	The new variant has a gap of 22 amino acids between residues 146 – 169. The new variant maintains the active site and site important for substrate recognition.
APE1_HUMAN	NV-13	The new variant has an insertion of 25 amino acids after residue 18. The new variant maintains the active site and site important for substrate recognition.
MAD3_HUMAN	NV-14	The new variant has an alternative 3' exon of 3 amino acids instead of 15 amino acids. It retains all five ANK motifs and the two PHOSPHORYLATION sites.
MAD3_HUMAN	NV-15	The new variant has a deletion of 28 amino acids between 183 – 212. The deletion is in the ANK MOTIF 4. The new variant maintains 4 out of the five ANK MOTIFs and the two PHOSPHORYLATION sites.
EPA4_HUMAN	NV-16	Deletion of 65aa after residue 832 (832-898). Deletion in end of CYTOPLASMIC domain. The 3' end of the PROTEIN KINASE domain is missing, but all important sites are maintained. The new variant has two FYBRONECTIN TYPE III domains and the protein KINASE domain with 2 ATP binding sites, an ACTIVE site and an auto PHOSPHORYLATION site.

ETS2_HUMAN	NV-17	The new variant has a deletion of 26 aa between 87 - 114. The new variant maintains the DNA binding domain.
WN5A_HUMAN 1.	NV-18	The new variant has an alternative 3' exon of 4 amino acids instead of 109. It is identical to the known protein until residue 256. Two GLYCOSILATION sites out of four are missing in the new variant.
TYO3_HUMAN	NV-19	The new variant has an alternative 3' exon of 45 amino acids instead of 216 amino acids. The new variant is missing part of the PROTEIN KINASE domain and its AUTOPHOSPHORYLATION site. However, it maintains all other necessary domains: the ACTIVE site and the two ATP binding sites. The variant retains all 6 GLYCOSILATION sites, the 2 IG-like domains and the 2 FIBRONEXTIN TYPE III domains.
CAD2_HUMAN	NV-20	The new variant has an alternative 3' exon of 10 amino acids instead of 68 amino acids. The new variant maintains the extracellular domain and the TM domain. It is missing the end of the cytoplasmic domain and the SER-RICH domain. However, it has all other necessary domains including :5 CADHERIN REPEATS with 7 GLYCOSILATION sites.
MXI1_HUMAN	NV-21	NV_1 m85527_3 Insertion of 24aa after residue 79. Most likely truncated in insertion. Has basic DNA binding domain, but lacks helix-loop-helix.
MXI1_HUMAN	NV-22	NV_2 m85527_5 Alternative 5' exon. Identical to known from aa 26 to the end. Has a 5' exon of 31 aa versus 25 aa of the known. Has both DNA binding domain and

		helix loop helix. The alternative 5' exon bares a clathrin repeat. Supported by 4 ests.
MPK3_HUMAN	NV-23	Similar to known RNA at first 290 aa. Alternative 3' exon of 10 aa instead of 28 The new variant maintains the PROTEIN KINASE domain with its two ATP binding sites, the ACTIVE site and two POSPHORYLATION sites.
XRC1_HUMAN	NV-24	First 242aa identical to known RNA. Alternative short 3' exon of 50 aa Instead of 391aa.
XRC1_HUMAN	NV-25	Identical to known RNA in first 241 aa. Alternative 3' exon of 25 aa instead of 392.
XRC1_HUMAN	NV-26	Identical to known RNA in first 186 aa. Alternative short 3' exon of length 61 aa, instead of 447 aa.
XRC1_HUMAN	NV-27	Identical to known RNA in first 540 aa. Alternative 3' exon of 84 aa instead of 93 aa.
MERL_HUMAN	NV-28	Deletion of 29 aa from position 333. The new variant retains the Band 4-1 like domain. (Band 4.1, which links the spectrin-actin cytoskeleton of erythrocytes to the plasma membrane.)
DP1_HUMAN	NV-29	Alternative 3' exon of 21 amino acids instead of 72 amino acids. The new variant retains the two transmembrane domains.
MDR1_HUMAN	NV-30	Alternative exon at 3' end at cytoplasmic domain. 1 aa instead of 3 of the known. Identical to known until aa 1277.
MDR1_HUMAN	NV-31	The new variant is a truncated protein. It has an alternative 3' exon of 12 amino acids instead of 713. It is

		identical to the known protein until residue 567. The new variant retains only one out of two ATP binding sites, and six out of twelve TM domains. It has one out of three cytoplasmic domains and is truncated in the middle of the second cytoplasmic domain.
MK08_HUMAN	NV-32	Identical to known until aa 205. Truncated. Has additional 13 aa. Lacks part of the protein kinase domain. Retains the active site the two ATP binding sites and the two phosphorylation sites.
MK08_HUMAN	NV-33	Alternative 3' exon of 14 aa instead of 134 aa. Identical to known until residue 293. Lacks end of protein kinase domain. Retains the active site, the two ATP binding sites and the two phosphorylation sites.
MK08_HUMAN	NV-34	Alternative 3' exon of 7 aa instead of 95 aa. Identical to known until residue 332. Has entire protein kinase domain including the active site, the two ATP binding sites and the two phosphorylation sites.
MAPK12_HUMAN	NV-35	The new variant contains 152 N-terminal amino acids of the original protein. The new variant has alternative 25 amino acids in its C-terminus, instead of original 215 amino acids. It contains the NP_BIND (between the amino acids 33 – 41, and the ATP binding site at position 56. The truncated variant has only part of the kinase domain, it lacks the active site and both the phosphorylation sites that activates the kinase. . This truncated splice variant can act as dominant negative.
KPCT_HUMAN	NV-36	The new variant has an alternative 3′ exon of 36 amino acids instead of 94 original amino acids. The alternative region is in the PROTEIN KINASE domain. The new variant maintains

		the two PHORBOL-ESTER AND DAG BINDING domains, the two ATP binding sites and the ACTIVE of the KINASE domain.

The following is a list of the original tumor-involved sequences, followed by all the splice variants obtained therefrom with a list of differences between the original TIG sequence and the variant.

KU (p70/p80)

KU70_HUMAN

FUNCTION: SINGLE STRANDED DNA-DEPENDENT ATP-DEPENDENT HELICASE. HAS A ROLE IN CHROMOSOME TRANSLOCATION. THE DNA HELICASE II COMPLEX BINDS PREFERENTIALLY TO FORK-LIKE ENDS OF DOUBLE-STRANDED DNA IN A CELL CYCLE-DEPENDENT MANNER. IT WORKS IN THE 3'-5' DIRECTION. BINDING TO DNA MAY BE MEDIATED BY P70.
SUBUNIT: HETERODIMER OF A 70 KD AND A 80 KD SUBUNIT.
SUBCELLULAR LOCATION: NUCLEAR.
PTM: PHOSPHORYLATED IN VIVO AT SERINE RESIDUES (BY SIMILARITY).
DISEASE: INDIVIDUALS WITH SLE AND RELATED DISORDERS PRODUCE EXTREMELY LARGE AMOUNTS OF AUTOANTIBODIES TO P70 AND P86. EXISTENCE OF A MAJOR AUTOANTIGENIC EPITOPE OR EPITOPES ON THE CARBOXY TERMINAL 190 AMINO ACIDS OF P70 CONTAINING THE LEUCINE REPEAT. THE MAJORITY OF AUTOANTIBODIES TO P70 IN MOST SERA FROM PATIENTS WITH SLE SEEM TO BE REACTIVE WITH THIS REGION.
SIMILARITY: BELONGS TO THE ATP-DEPENDENT DNA HELICASE II 70 KD SUBUNIT FAMILY.

NV_1

The new variant has an alternative 3' exon of 5 amino acids instead of 240 amino acids. It is probably missing the PHOSPHORYLATION (BY NUCLEAR

KINASE NII) site and half of the PRO-RICH domain but retains the LEUCINE-ZIPPER domain.

KU (p70/p80)

KU70_HUMAN

NV_2

The new variant has a deletion of 210 amino acids between residues 304 – 515. The new variant lacks the PRO-RICH domain but retains the LEUCINE-ZIPPER domain and PHOSPHORYLATION (BY NUCLEAR KINASE NII) site.

LCK

LCK_HUMAN

PROTO-ONCOGENE TYROSINE-PROTEIN KINASE LCK
FUNCTION: MAY PARTICIPATE IN ANTIGEN-INDUCED T-CELL ACTIVATION.
CATALYTIC ACTIVITY: ATP + A PROTEIN TYROSINE = ADP + PROTEIN TYROSINE PHOSPHATE.
ENZYME REGULATION: REGULATED BY PHOSPHORYLATION ON TYR-504.
SUBCELLULAR LOCATION: BOUND TO THE CYTOPLASMIC DOMAIN OF EITHER CD4 OR CD8.
SIMILARITY: CONTAINS 1 SH2 DOMAIN.
SIMILARITY: CONTAINS 1 SH3 DOMAIN.
SIMILARITY: TO OTHER PROTEIN-TYROSINE KINASES IN THE CATALYTIC DOMAIN. BELONGS TO THE SRC SUBFAMILY.

NV_3

The new variant has an alternative 3' exon of 45 amino acids instead of 163 amino acids. The new variant retains both SH domains and most of the PROTEIN KINASE domain including two ATP BINDING sites and the

ACTIVE SITE. It is missing the 3' end of the PROTEIN KINASE domain and lacks the AUTO-PHOSPHORYLATION and PHOSPHORYLATION sites.

LCK

LCK_HUMAN

NV_4

Insertion of 58 amino acids after amino acid 62 (insertion does not result in truncation). Insertion in first SH2 domain. The new variant retains all important sites including: the PROTEIN KINASE DOMAIN with two ATP BINDING sites, an ACTIVE SITE and an AUTO PHOSPHORYLATION site. An additional PHOSPHORYLATION site.

OSTEOPONTIN

OSTP_HUMAN

FUNCTION: BINDS TIGHTLY TO HYDROXYAPATITE. APPEARS TO FORM AN INTEGRAL PART OF THE MINERALIZED MATRIX. PROBABLY IMPORTANT TO CELL-MATRIX INTERACTION.
ALTERNATIVE PRODUCTS: TWO ISOFORMS; OP1A AND OP1B (SHOWN HERE); ARE PRODUCES BY ALTERNATIVE SPLICING.
PTM: EXTENSIVELY PHOSPHORYLATED ON SERINE RESIDUES.
PTM: N- AND O-GLYCOSYLATED.
DISEASE: THIS PROTEIN PLAYS A PRINCIPAL ROLE IN URINARY STONE FORMATION AS THE STONE MATRIX

NV_5

The new variant has an alternative 3' exon of 12 amino acids instead of 134 amino acids. The new variant maintains the CELL ATTACHMENT SITE and two GLYCOSILATION sites.

GADD45

GA45_HUMAN

GROWTH ARREST AND DNA-DAMAGE-INDUCIBLE PROTEIN
FUNCTION: INVOLVED IN THE REGULATION OF GROWTH AND APOPTOSIS. MEDIATES ACTIVATION OF STRESS-RESPONSIVE MTK1/MEKK4 MAPKKK.
SIMILARITY: BELONGS TO THE GADD45 / MYD118 FAMILY.

NV_6

The new variant has an alternative 5' exon of 72 amino acids instead of 125 amino acids. The new variant has a signal peptide and has the two PHOSPHORYLATION (BY CK2) sites.

WNT-11 PROTEIN

WN11_HUMAN

FUNCTION: PROBABLE DEVELOPMENTAL PROTEIN. MAY BE A SIGNALING MOLECULE WHICH AFFECT THE DEVELOPMENT OF DISCRETE REGIONS OF TISSUES. IS LIKELY TO SIGNAL OVER ONLY FEW CELL
DIAMETERS.
SUBCELLULAR LOCATION: POSSIBLY SECRETED AND ASSOCIATES WITH THE EXTRACELLULAR MATRIX.
SIMILARITY: BELONGS TO THE WNT FAMILY

NV_7

The new variant has a deletion of 22 amino acids after residue 312 (between 312-334). The new variant has all five potential GLYCOSILATION sites.

WNT-11 PROTEIN

WN11_HUMAN

NV_8

The new variant has a deletion of 117 amino acids after residue 116 (between 116-233). The new variant is missing one potential GLYCOSILATION site (out of 5 sites).

PROTEIN KINASE C, THETA TYPE

KPCT_HUMAN

FUNCTION: THIS IS CALCIUM-INDEPENDENT, PHOSPHOLIPID-DEPENDENT, SERINE- AND THREONINE-SPECIFIC ENZYME.
FUNCTION: PKC IS ACTIVATED BY DIACYLGLYCEROL WHICH IN TURN PHOSPHORYLATES A RANGE OF CELLULAR PROTEINS. PKC ALSO SERVES AS THE RECEPTOR FOR PHORBOL ESTERS, A CLASS OF TUMOR
PROMOTERS.
TISSUE SPECIFICITY: SKELETAL MUSCLE, MEGAKARYOBLASTIC CELLS AND PLATELETS.
SIMILARITY: CONTAINS 2 ZINC-DEPENDENT PHORBOL-ESTER AND DAG BINDING DOMAINS.
SIMILARITY: BELONGS TO THE SER/THR FAMILY OF PROTEIN KINASES. PKC SUBFAMILY.

NV_9

The new variant has an alternative 3' exon of 3 amino acids instead of 94 amino acids. The alternative region is in the PROTEIN KINASE domain. The new variant maintains the two PHORBOL-ESTER AND DAG BINDING domains, the two ATP binding sites and the ACTIVE of the KINASE domain.

INTERFERON REGULATORY FACTOR 1

IRF1_HUMAN

FUNCTION: SPECIFICALLY BINDS TO THE UPSTREAM REGULATORY REGION OF TYPE I IFN AND IFN-INDUCIBLE MHC CLASS I GENES (THE INTERFERON CONSENSUS SEQUENCE (ICS)) AND ACTIVATES THOSE GENES.
SUBCELLULAR LOCATION: NUCLEAR.
INDUCTION: BY VIRUSES AND IFN.
DISEASE: DELETION OR REARRANGEMENT OF IRF1 ARE A CAUSE OF PRELEUKEMIC MYELODYSPLASTIC SYNDROME (MDS) AND OF ACUTE MYELOGENOUS LEUKEMIA (AML).
SIMILARITY: BELONGS TO THE IRF FAMILY.

NV_10

The new variant has an alternative 3' exon of 7 amino acids instead of 40 amino acids. The new variant maintains the DNA binding domain.

BASIC FIBROBLAST GROWTH FACTOR RECEPTOR 1

FGR1_HUMAN

FUNCTION: RECEPTOR FOR BASIC FIBROBLAST GROWTH FACTOR. A SHORTER FORM OF THE RECEPTOR COULD BE A RECEPTOR FOR ACIDIC FGF (AFGF).
CATALYTIC ACTIVITY: ATP + PROTEIN TYROSINE = ADP + PROTEIN TYROSINE PHOSPHATE.
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.
ALTERNATIVE PRODUCTS: MANY FORMS OF FGFR1 ARE PRODUCED BY ALTERNATIVE SPLICING. THE FORM SHOWN HERE IS KNOWN AS ALPHA-A1.
DISEASE: DEFECTS IN FGFR1 ARE ONE OF THE CAUSES OF PFEIFFER SYNDROME, ALSO CALLED ACROCEPHALOSYNDACTYLY TYPE V (ACS V), CHARACTERIZED BY CRANIOSYNOSTOSIS (PREMATURE FUSION OF THE SKULL SUTURES) WITH DEVIATION AND ENLARGEMENT OF THE THUMBS AND GREAT

TOES,BRACHYMESOPHALANGY, WITH PHALANGEAL ANKYLOSIS AND A VARYING DEGREE OF SOFT TISSUE SYNDACTYLY.
SIMILARITY: BELONGS TO THE FIBROBLAST GROWTH FACTOR RECEPTOR FAMILY.
SIMILARITY: CONTAINS 3 IMMUNOGLOBULIN-LIKE DOMAINS.

NV_11

The new variant has an alternative 3' exon of 14 amino acids instead of 134 amino acids. The new variant has the entire extracellular domain and the TM, it is missing part of the cytoplasmic domain. The new variant maintains all 3 IMMUNOGLOBULIN-LIKE DOMAINS, the protein KINASE domain, the ACTIVE site, and the 2 ATP binding sites, but it might be missing one of the two PHOSPHORYLATION (AUTO-) sites.

REF-1 PROTEIN DNA-(APURINIC OR APYRIMIDINIC SITE) LYASE APE1_HUMAN

FUNCTION: REPAIRS OXIDATIVE DNA DAMAGES IN VITRO. MAY HAVE A ROLE IN PROTECTION AGAINST CELL LETHALITY AND SUPPRESSION OF MUTATIONS. REMOVES THE BLOCKING GROUPS FROM THE 3'
TERMINI OF THE DNA STRAND BREAKS GENERATED BY IONIZING RADIATIONS AND BLEOMYCIN.
CATALYTIC ACTIVITY: ENDONUCLEOLYTIC CLEAVAGE NEAR APURINIC OR APYRIMIDINIC SITES TO PRODUCTS WITH 5'-PHOSPHATE.
SUBCELLULAR LOCATION: NUCLEAR.
SIMILARITY: BELONGS TO THE AP/EXOA FAMILY OF DNA REPAIR ENZYMES.

NV_12

The new variant has a gap of 22 amino acids between residues 146 – 169. The new variant maintains the ACTIVE site and site important for substrate recognition.

NV_13

The new variant has an insertion of 25 amino acids after residue 18.It maintains the ACTIVE site and the site important for substrate recognition.

MAD3 MAJOR HISTOCOMPATIBILITY COMPLEX ENHANCER-BINDING PROTEIN

MAD3_HUMAN

FUNCTION: I-KAPPA-B-LIKE ACTIVITY. MAY BE INVOLVED IN REGULATION OF TRANSCRIPTIONAL RESPONSES TO NF-KAPPA-B, INCLUDING ADHESION- DEPENDENT PATHWAYS OF MONOCYTE ACTIVATION. INTERACTS DIRECTLY WITH THE NF-KAPPA-B COMPLEX, PRESUMABLY THROUGH THE P65 SUBUNIT.
INDUCTION: INDUCED IN ADHERENT MONOCYTES.
PTM: PHOSPHORYLATION OF I-KAPPA-B BLOCKS ITS ABILITY TO INHIBIT NF-KAPPA-B DNA-BINDING ACTIVITY.
SIMILARITY: CONTAINS 5 ANK REPEATS.

NV_14

The new variant has an alternative 3' exon of 3 amino acids instead of 15 amino acids. It retains all five ANK motifs and the two PHOSPHORYLATION sites.

NV_15

The new variant has a deletion of 28 amino acids between 183 – 212. The deletion is in the ANK MOTIF 4.The new variant maintains 4 out of the five ANK MOTIFs and the two PHORYLATION sites.

RECEPTOR PROTEIN-TYROSINE KINASE HEK8

EPA4_HUMAN

FUNCTION: RECEPTOR FOR MEMBERS OF THE EPHRIN-A FAMILY. BINDS TO EPHRIN-A1, -A4 AND -A5. BINDS MORE POORLY TO EPHRIN-A2 AND A-3.
CATALYTIC ACTIVITY: ATP + A PROTEIN TYROSINE = ADP + PROTEIN TYROSINE PHOSPHATE.
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.
SIMILARITY: CONTAINS 2 FIBRONECTIN TYPE III-LIKE DOMAINS.
SIMILARITY: TO OTHER PROTEIN-TYROSINE KINASES IN THE CATALYTIC DOMAIN. BELONGS TO THE EPHRIN RECEPTOR FAMILY.

NV_16

Deletion of 65 amino acids between 832 – 898. The deletion in the cytoplasmic domain. The 3' end of the PROTEIN KINASE domain is missing, but all important sites are maintained. The new variant has two FYBRONECTIN TYPE III domains and the protein KINASE domain with 2 ATP binding sites, an ACTIVE site and an auto PHOSPHORYLATION site.

C-ETS-2 PROTEIN

ETS2_HUMAN

SUBCELLULAR LOCATION: NUCLEAR.
SIMILARITY: BELONGS TO THE ETS FAMILY.

NV_17

The new variant has a deletion of 26 amino acids between 87 – 114. The new variant maintains the DNA binding domain.

WNT-5A PROTEIN

WN5A_HUMAN

FUNCTION: PROBABLE DEVELOPMENTAL PROTEIN. MAY BE A SIGNALING MOLECULE WHICH AFFECTS THE DEVELOPMENT OF DISCRETE REGIONS OF TISSUES. IS LIKELY TO SIGNAL OVER ONLY FEW CELL DIAMETERS.
SUBCELLULAR LOCATION: POSSIBLY SECRETED AND ASSOCIATES WITH THE EXTRACELLULAR MATRIX.
SIMILARITY: BELONGS TO THE WNT FAMILY

NV_18

The new variant has an alternative 3' exon of 4 amino acids instead of 109. It is identical to the known protein until residue 256. Two GLYCOSILATION sites out of four are missing in the new variant.

TYROSINE-PROTEIN KINASE SKY

TYO3_HUMAN

FUNCTION: MAY BE INVOLVED IN CELL ADHESION PROCESSES, PARTICULARLY IN THE CENTRAL NERVOUS SYSTEM.
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.
TISSUE SPECIFICITY: ABUNDANT IN THE BRAIN AND LOWER LEVELS IN OTHER TISSUES.
SIMILARITY: TO OTHER PROTEIN-TYROSINE KINASES IN THE CATALYTIC DOMAIN.
SIMILARITY: CONTAINS 2 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAINS.
SIMILARITY: CONTAINS 2 FIBRONECTIN TYPE III-LIKE DOMAINS.

NV_19

The new variant has an alternative 3' exon of 45 amino acids instead of 216 amino acids. The new variant is missing part of the PROTEIN KINASE domain and its AUTOPHOSPHORYLATION site. However, it maintains all other necessary domains: the ACTIVE site and the two ATP binding sites. The variant retains all 6 GLYCOSILATION sites, the 2 IG-like domains and the 2 FIBRONEXTIN TYPE III domains.

NEURAL-CADHERIN

CAD2_HUMAN

FUNCTION: CADHERINS ARE CALCIUM DEPENDENT CELL ADHESION PROTEINS. THEY PREFERENTIALLY INTERACT WITH THEMSELVES IN A HOMOPHILIC MANNER IN CONNECTING CELLS; CADHERINS MAY THUS CONTRIBUTE TO THE SORTING OF HETEROGENEOUS CELL TYPES. N-CADHERIN MAY BE INVOLVED IN NEURONAL RECOGNITION MECHANISM.
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.
SIMILARITY: BELONGS TO THE CADHERIN FAMILY.

NV_20

The new variant has an alternative 3' exon of 10 amino acids instead of 68 amino acids. The new variant maintains the extracellular domain and the TM domain. It is missing the end of the cytoplasmic domain and the SER-RICH domain. However, it has all other necessary domains including: 5 CADHERIN REPEATS with 7 GLYCOSILATION sites.

MXI1 MAX INTERACTING PROTEIN 1

MXI1_HUMAN

FUNCTION: TRANSCRIPTIONAL REPRESSOR. MXI1 BINDS WITH MAX TO FORM A SEQUENCE-SPECIFIC DNA-BINDING PROTEIN COMPLEX

WHICH RECOGNIZES THE CORE SEQUENCE 5'-CAC[GA]TG-3'. MXI1 THUS ANTAGONIZES MYC TRANSCRIPTIONAL ACTIVITY BY COMPETING FOR MAX.
SUBUNIT: EFFICIENT DNA BINDING REQUIRES DIMERIZATION WITH ANOTHER BHLH PROTEIN.BINDS DNA AS A HETERODIMER WITH MAX.
SUBCELLULAR LOCATION: NUCLEAR.
TISSUE SPECIFICITY: HIGH LEVELS FOUND IN THE BRAIN, HEART AND LUNG WHILE LOWER LEVELS ARE SEEN IN THE LIVER, KIDNEY AND SKELETAL MUSCLE.
DISEASE: DEFECTS IN MXI1 ARE FOUND IN SOME PATIENTS WITH PROSTATE TUMORS.
SIMILARITY: BELONGS TO THE BASIC HELIX-LOOP-HELIX (BHLH) FAMILY OF TRANSCRIPTION FACTORS.

NV_21

The new variant has an insertion of 24 amino acids after residue 79. It is most likely truncated within the insertion. The new variant retains the BASIC DNA BINDING domain, but lacks the HELIX LOOP HELIX motif.

MXI1 MAX INTERACTING PROTEIN 1

MXI1_HUMAN

NV_22

The new variant has an alternative 5' exon of 31 amino acids instead of 25. It is identical to the known protein from residue 26 to the end. The new variant has both the DNA BINDING DOMAIN and the HELIX LOOP HELIX motif. The alternative 5' exon bares a clathrin repeat.

DUAL SPECIFICITY MITOGEN-ACTIVATED PROTEIN KINASE KINASE 3

MPK3_HUMAN

FUNCTION: DUAL SPECIFICITY KINASE. IS ACTIVATED BY CYTOKINES AND ENVIRONMENTAL STRESS IN VIVO. CATALYZES THE CONCOMITANT PHOSPHORYLATION OF A THREONINE AND A TYROSINE RESIDUE IN THE MAP KINASE P38.
ENZYME REGULATION: ACTIVATED BY DUAL PHOSPHORYLATION ON SER-189 AND THR-193.
TISSUE SPECIFICITY: ABUNDANT EXPRESSION IS SEEN IN THE SKELETAL MUSCLE. IT IS ALSO WIDELY EXPRESSED IN OTHER TISSUES.
PTM: AUTOPHOSPHORYLATED.
SIMILARITY: BELONGS TO THE SER/THR FAMILY OF PROTEIN KINASES. MAP KINASE KINASE SUBFAMILY.

NV_23

The new variant has an alternative 3' exon of 10 amino acids instead of 28 amino acids. The new variant maintains the PROTEIN KINASE domain with its two ATP binding sites, the ACTIVE site and two POSPHORYLATION sites.It may lack a few amino acids at the end of the PROTEIN KINASE domain.

DNA-REPAIR PROTEIN XRCC1

XRC1_HUMAN

FUNCTION: CORRECTS DEFECTIVE DNA STRAND-BREAK REPAIR AND SISTER CHROMATID EXCHANGE FOLLOWING TREATMENT WITH IONIZING RADIATION AND ALKYLATING AGENTS.
SUBCELLULAR LOCATION: NUCLEAR (PROBABLE).
SIMILARITY: SOME, TO S.POMBE RAD4/CUT5.

NV_24

Alternative 3' exon of 50 amino acids instead of 391 amino acids.

DNA-REPAIR PROTEIN XRCC1

XRC1_HUMAN

NV_25

Alternative 3' exon of 25 amino acids instead of 392 amino acids.

DNA-REPAIR PROTEIN XRCC1

XRC1_HUMAN

NV_26

Alternative 3' exon of 61 amino acids instead of 447 amino acids.

DNA-REPAIR PROTEIN XRCC1

XRC1_HUMAN

NV_27

Alternative 3' exon of 84 amino acids instead of 93 amino acids.

MERLIN SCHWANNOMIN (NF2)

MERL_HUMAN

FUNCTION: PROBABLY ACTS AS A MEMBRANE STABILIZING PROTEIN.
TISSUE SPECIFICITY: IN FETAL BRAIN; IN KIDNEY, LUNG, BREAST, AND OVARY.
DISEASE: NEUROFIBROMATOSIS 2 (NF2) OR CENTRAL NEUROFIBROMATOSIS IS A GENETIC DISORDER CHARACTERIZED BY BILATERAL VESTIBULAR SCHWANNOMAS (FORMERLY CALLED

ACOUSTIC NEUROMAS), SCHWANNOMAS OF OTHER CRANIAL AND PERIPHERAL NERVES,MENINGIOMAS, AND EPENDYMOMAS. IT IS INHERITED IN AN AUTOSOMAL DOMINANT FASHION WITH FULL PENETRANCE. AFFECTED INDIVIDUALS GENERALLY DEVELOP SYMPTOMS
OF EIGHTH-NERVE DYSFUNCTION IN EARLY ADULTHOOD, INCLUDING DEAFNESS AND BALANCE DISORDER. ALTHOUGH THE TUMORS OF NF2 ARE HISTOLOGICALLY BENIGN, THEIR ANATOMIC LOCATION MAKES MANAGEMENT DIFFICULT, AND PATIENTS SUFFER GREAT MORBIDITY AND MORTALITY.
SIMILARITY: CONTAINS A DOMAIN FOUND IN BAND 4.1, EZRIN, MOESIN, RADIXIN, AND TALIN.

NV_28

The new variant has a deletion of 29 amino acids after residue 333.The new variant maintains the BAND 4,1 – LIKE domain. (Band 4.1, which links the spectrin-actin cytoskeleton of erythrocytes to the plasma membrane).

DP1 POLYPOSIS LOCUS PROTEIN 1

DP1_HUMAN

SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN (POTENTIAL).
SIMILARITY: TO C.ELEGANS T19C3.4.

NV_29

Alternative 3' exon of 21 amino acids instead of 72 amino acids. The new variant maintains the two transmembrane domains.

MDR1 MULTIDRUG RESISTANCE PROTEIN 1

MDR1_HUMAN

FUNCTION: ENERGY-DEPENDENT EFFLUX PUMP RESPONSIBLE FOR DECREASED DRUG ACCUMULATION IN MULTIDRUG-RESISTANT CELLS.
SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN.
SIMILARITY: BELONGS TO THE ATP-BINDING TRANSPORT PROTEIN FAMILY (ABC TRANSPORTERS). MDR SUBFAMILY.

NV_30

The new variant has an alternative 3' exon of 1 amino acid, instead of 3 of the known protein. The new variant is identical to the known protein until residue 1277. It maintains all important sites.

MDR1 MULTIDRUG RESISTANCE PROTEIN 1

MDR1_HUMAN

NV_31

The new variant is a truncated protein. It has an alternative 3' exon of 12 amino acids instead of 713. It is identical to the known protein until residue 567. The new variant retains only one out of two ATP binding sites, and six out of twelve TM domains. It has one out of three cytoplasmic domains and is truncated in the middle of the second cytoplasmic domain.

JNK1 – MITOGEN ACTIVATED PROTEIN KINASE 8

MK08_HUMAN

FUNCTION: PROBABLY PLAYS A ROLE IN THE SIGNAL TRANSDUCTION PATHWAY INITIATED BY PROINFLAMMATORY CYTOKINES AND UV RADIATION. BINDS TO THE N-TERMINAL ACTIVATION DOMAINS OF C-JUN AND ATF2 AND PHOSPHORYLATES

THEIR REGULATORY SITES (RESPECTIVELY SER-63 AND SER-73; THR-69 AND THR-71). JNK1 ISOFORMS DISPLAY DIFFERENT BINDING PATTERNS: BETA-1 PREFERENTIALLY BINDS TO C-JUN, WHEREAS ALPHA-1, ALPHA-2, AND BETA-2 HAVE A SIMILAR LOW LEVEL OF BINDING TO BOTH C-JUN OR ATF2. HOWEVER THERE IS NO CORRELATION BETWEEN BINDING AND PHOSPHORYLATION, WHICH IS ACHIEVED ABOUT AT THE SAME EFFICIENCY BY ALL ISOFORMS.
ENZYME REGULATION: ACTIVATED BY THREONINE AND TYROSINE PHOSPHORYLATION.
ALTERNATIVE PRODUCTS: FOUR ISOFORMS JNK1 ALPHA-1, JNK1 ALPHA-2 (SHOWN HERE), JNK1 BETA-1, AND JNK1 BETA-2 ARE PRODUCED BY ALTERNATIVE SPLICING.
INDUCTION: BY UV LIGHT, INTERLEUKIN-1 AND BY HA-RAS.
SIMILARITY: BELONGS TO THE CDC2/CDC28 SUBFAMILY OF SER/THR PROTEIN KINASES. STRONGEST SIMILARITY WITH OTHER MAP KINASES.

NV_32

The new variant is a truncated protein. It has an alternative 3' exon of 13 amino acids instead of 222 amino acids. It is identical to the known protein until residue 205. The new variant lacks part of the PROTEIN KINASE domain, however it retains the ACTIVE SITE, the two ATP binding sites and the two PHOSPHORYLATION sites.

JNK1 – MITOGEN ACTIVATED PROTEIN KINASE 8
MK08_HUMAN

NV_33

The new variant has an alternative 3' exon of 14 amino acids instead of 134 amino acids of the known protein. It is identical to the known protein until residue 293. The new variant lacks the end of the PROTEIN KINASE domain, but retains the ACTIVE SITE, the two ATP binding sites and the two PHOSPHORYLATION sites.

JNK1 – MITOGEN ACTIVATED PROTEIN KINASE 8
MK08_HUMAN

NV_34

The new variant has an alternative 3' exon of 7 amino acids a instead of 95 amino acids. It is identical to the known protein until residue 332. Has the entire PROTEIN KINASE domain including the ACTIVE SITE, the two ATP binding sites and the two PHOSPHORYLATION sites.

MITOGEN-ACTIVATED PROTEIN KINASE 12

Synonym(s) EC 2.7.1- extracellular signal-regulated kinase 6 EC 2.7.1- ERK 6 ERK 5 stress-activated protein kinase-3 mitogen-activated protein kinase P38 gamma map kinase P38 gamma

Gene name(s) MAPK12 or ERK 6 or SAPK 3

FUNCTION: PHOSPHORYLATES MYELIN BASIC PROTEIN (MBP); ACTS AS SIGNAL TRANSDUCER DURING THE DIFFERENTIATION OF MYOBLASTS TO MYOTUBES. OVEREXPRESSION ENHANCES THIS DIFFERENTIATION EVENT, WHEREAS INACTIVATION EXHIBITS IT AND MAINTAINS THE CELLS IN A PROLIFERATIVE STATE.

ENZYME REGULATION: ACTIVATED BY PHSOPHORYLATION ON THREONINE AND TYROSINE (BY SIMILARITY).

TISSUE SPECIFICITY: HIGHLY EXPRESSED IN SKELETAL MUSCLE.

SIMILARITY: BELONGS TO THE SER/THR FAMILY OF PROTEIN KINASES. MAP KINASE FAMILY.

NV_35

The new variant contains 152 N-terminal amino acids of the original protein. The new variant has alternative 25 amino acids in its C-terminus, instead of original 215 amino acids. It contains the NP_BIND (between the amino acids 33 – 41, and the ATP binding site at position 56. The truncated variant has only part of the kinase domain, it lacks the active site and both the phosphorylation sites that activates the kinase. This truncated splice variant can act as dominant negative.

PROTEIN KINASE C, THETA TYPE
KPCT_HUMAN

FUNCTION: THIS IS CALCIUM-INDEPENDENT, PHOSPHOLIPID-DEPENDENT, SERINE- AND THREONINE-SPECIFIC ENZYME.
FUNCTION: PKC IS ACTIVATED BY DIACYLGLYCEROL WHICH IN TURN PHOSPHORYLATES A RANGE OF CELLULAR PROTEINS. PKC ALSO SERVES AS THE RECEPTOR FOR PHORBOL ESTERS, A CLASS OF TUMOR PROMOTERS.
TISSUE SPECIFICITY: SKELETAL MUSCLE, MEGAKARYOBLASTIC CELLS AND PLATELETS.
SIMILARITY: CONTAINS 2 ZINC-DEPENDENT PHORBOL-ESTER AND DAG BINDING DOMAINS.
SIMILARITY: BELONGS TO THE SER/THR FAMILY OF PROTEIN KINASES. PCK SUBFAMILY.

NV_36

The new variant has an alternative 3′ exon of 36 amino acids instead of 94 original amino acids. The alternative region is in the PROTEIN KINASE domain. The new variant maintains the two PHORBOL-ESTER AND DAG BINDING domains, the two ATP binding sites and the ACTIVE of the KINASE domain.

Example II: Variant nucleic acid sequence

The nucleic acid sequences of the invention include nucleic acid sequences which encode variant product and fragments and analogs thereof. The nucleic acid sequences may alternatively be sequences complementary to the above coding sequence, or to a region of said coding sequence. The length of the complementary sequence is sufficient to avoid the expression of the coding sequence. The nucleic acid sequences may be in the form of RNA or in the form of DNA, and include messenger RNA, synthetic RNA and DNA, cDNA, and genomic DNA. The DNA may be double-stranded or single-stranded, and if single-stranded may be the coding strand or the non-coding (anti-sense, complementary) strand. The nucleic acid sequences may also both include dNTPs, rNTPs as well as non naturally occurring sequences. The sequence may also be a part of a hybrid between an amino acid sequence and a nucleic acid sequence.

In a general embodiment, the nucleic acid sequence has at least 90%, identity with any one of the sequence identified as SEQ ID NO: 1 to SEQ ID NO: 36 provided that this sequence is not completely identical with that of the original sequence.

The nucleic acid sequences may include the coding sequence by itself. By another alternative the coding region may be in combination with additional coding sequences, such as those coding for fusion protein or signal peptides, in combination with non-coding sequences, such as introns and control elements, promoter and terminator elements or 5' and/or 3' untranslated regions, effective for expression of the coding sequence in a suitable host, and/or in a vector or host environment in which the variant nucleic acid sequence is introduced as a heterologous sequence.

The nucleic acid sequences of the present invention may also have the product coding sequence fused in-frame to a marker sequence which allows for purification of the variant product. The marker sequence may be, for example, a

hexahistidine tag to provide for purification of the mature polypeptide fused to the marker in the case of a bacterial host, or, the marker sequence may be a hemagglutinin (HA) tag when a mammalian host, e.g. COS-7 cells, is used. The HA tag corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson, I., *et al. Cell* 37:767 (1984)).

Also included in the scope of the invention are fragments as defined above also referred to herein as oligonucleotides, typically having at least 20 bases, preferably 20-30 bases corresponding to a region of the coding-sequence nucleic acid sequence. The fragments may be used as probes, primers, and when complementary also as antisense agents, and the like, according to known methods.

As indicated above, the nucleic acid sequence may be substantially a depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 36 or fragments thereof or sequences having at least 90% identity to the above sequence as explained above. Alternatively, due to the degenerative nature of the genetic code, the sequence may be a sequence coding for any one of the amino acid sequence of SEQ ID NO: 37 to SEQ ID NO: 72, or fragments or analogs of said amino acid sequence.

A. Preparation of nucleic acid sequences

The nucleic acid sequences may be obtained by screening cDNA libraries using oligonucleotide probes which can hybridize to or PCR-amplify nucleic acid sequences which encode the variant products disclosed above. cDNA libraries prepared from a variety of tissues are commercially available and procedures for screening and isolating cDNA clones are well-known to those of skill in the art. Such techniques are described in, for example, Sambrook *et al.* (1989) Molecular Cloning: A Laboratory Manual (2nd Edition), Cold Spring Harbor Press, Plainview, N.Y. and Ausubel FM et al. (1989) Current Protocols in Molecular Biology, John Wiley & Sons, New York, N.Y.

The nucleic acid sequences may be extended to obtain upstream and downstream sequences such as promoters, regulatory elements, and 5' and 3'

untranslated regions (UTRs). Extension of the available transcript sequence may be performed by numerous methods known to those of skill in the art, such as PCR or primer extension (Sambrook *et al., supra*), or by the RACE method using, for example, the Marathon RACE kit (Clontech, Cat. # K1802-1).

Alternatively, the technique of *"restriction-site"* PCR (Gobinda *et al. PCR Methods Applic.* **2**:318-22, (1993)), which uses universal primers to retrieve flanking sequence adjacent a known locus, may be employed. First, genomic DNA is amplified in the presence of primer to a linker sequence and a primer specific to the known region. The amplified sequences are subjected to a second round of PCR with the same linker primer and another specific primer internal to the first one. Products of each round of PCR are transcribed with an appropriate RNA polymerase and sequenced using reverse transcriptase.

Inverse PCR can be used to amplify or extend sequences using divergent primers based on a known region (Triglia, T. *et al.*, *Nucleic Acids Res.* **16**:8186, (1988)). The primers may be designed using OLIGO(R) 4.06 Primer Analysis Software (1992; National Biosciences Inc, Plymouth, Minn.), or another appropriate program, to be 22-30 nucleotides in length, to have a GC content of 50% or more, and to anneal to the target sequence at temperatures about 68-72°C. The method uses several restriction enzymes to generate a suitable fragment in the known region of a gene. The fragment is then circularized by intramolecular ligation and used as a PCR template.

Capture PCR (Lagerstrom, M. *et al., PCR Methods Applic.* **1**:111-19, (1991)) is a method for PCR amplification of DNA fragments adjacent to a known sequence in human and yeast artificial chromosome DNA. Capture PCR also requires multiple restriction enzyme digestions and ligations to place an engineered double-stranded sequence into a flanking part of the DNA molecule before PCR.

Another method which may be used to retrieve flanking sequences is that of Parker, J.D., *et al., Nucleic Acids Res.*, **19**:3055-60, (1991)). Additionally, one can use PCR, nested primers and PromoterFinder™ libraries to *"walk in"* genomic

DNA (PromoterFinder™; Clontech, Palo Alto, CA). This process avoids the need to screen libraries and is useful in finding intron/exon junctions. Preferred libraries for screening for full length cDNAs are ones that have been size-selected to include larger cDNAs. Also, random primed libraries are preferred in that they will contain more sequences which contain the 5' and upstream regions of genes.

A randomly primed library may be particularly useful if an oligo d(T) library does not yield a full-length cDNA. Genomic libraries are useful for extension into the 5' nontranslated regulatory region.

The nucleic acid sequences and oligonucleotides of the invention can also be prepared by solid-phase methods, according to known synthetic methods. Typically, fragments of up to about 100 bases are individually synthesized, then joined to form continuous sequences up to several hundred bases.

B. Use of variant nucleic acid sequence for the production of variant products

In accordance with the present invention, nucleic acid sequences specified above may be used as recombinant DNA molecules that direct the expression of variant products.

As will be understood by those of skill in the art, it may be advantageous to produce variant product-encoding nucleotide sequences possessing codons other than those which appear in any one of SEQ ID NO: 1 to SEQ ID NO: 36 which are those which naturally occur in the human genome. Codons preferred by a particular prokaryotic or eukaryotic host (Murray, E. *et al. Nuc Acids Res.*, 17:477-508, (1989)) can be selected, for example, to increase the rate of variant product expression or to produce recombinant RNA transcripts having desirable properties, such as a longer half-life, than transcripts produced from naturally occurring sequence.

The nucleic acid sequences of the present invention can be engineered in order to alter a variant product coding sequence for a variety of reasons, including but not limited to, alterations which modify the cloning, processing

and/or expression of the product. For example, alterations may be introduced using techniques which are well known in the art, e.g., site-directed mutagenesis, to insert new restriction sites, to alter glycosylation patterns, to change codon preference, etc.

The present invention also includes recombinant constructs comprising one or more of the sequences as broadly described above. The constructs comprise a vector, such as a plasmid or viral vector, into which a nucleic acid sequence of the invention has been inserted, in a forward or reverse orientation. In a preferred aspect of this embodiment, the construct further comprises regulatory sequences, including, for example, a promoter, operably linked to the sequence. Large numbers of suitable vectors and promoters are known to those of skill in the art, and are commercially available. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are also described in Sambrook, *et al., (supra)*.

The present invention also relates to host cells which are genetically engineered with vectors of the invention, and the production of the product of the invention by recombinant techniques. Host cells are genetically engineered (i.e., transduced, transformed or transfected) with the vectors of this invention which may be, for example, a cloning vector or an expression vector. The vector may be, for example, in the form of a plasmid, a viral particle, a phage, etc. The engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the expression of the variant nucleic acid sequence. The culture conditions, such as temperature, pH and the like, are those previously used with the host cell selected for expression, and will be apparent to those skilled in the art.

The nucleic acid sequences of the present invention may be included in any one of a variety of expression vectors for expressing a product. Such vectors include chromosomal, nonchromosomal and synthetic DNA sequences, e.g., derivatives of SV40; bacterial plasmids; phage DNA; baculovirus; yeast plasmids; vectors derived from combinations of plasmids and phage DNA, viral

DNA such as vaccinia, adenovirus, fowl pox virus, and pseudorabies. However, any other vector may be used as long as it is replicable and viable in the host. The appropriate DNA sequence may be inserted into the vector by a variety of procedures. In general, the DNA sequence is inserted into an appropriate restriction endonuclease site(s) by procedures known in the art. Such procedures and related sub-cloning procedures are deemed to be within the scope of those skilled in the art.

The DNA sequence in the expression vector is operatively linked to an appropriate transcription control sequence (promoter) to direct mRNA synthesis. Examples of such promoters include: LTR or SV40 promoter, the *E.coli lac* or *trp* promoter, the phage lambda *PL* promoter, and other promoters known to control expression of genes in prokaryotic or eukaryotic cells or their viruses. The expression vector also contains a ribosome binding site for translation initiation, and a transcription terminator. The vector may also include appropriate sequences for amplifying expression. In addition, the expression vectors preferably contain one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells such as dihydrofolate reductase or neomycin resistance for eukaryotic cell culture, or such as tetracycline or ampicillin resistance in *E.coli.*

The vector containing the appropriate DNA sequence as described above, as well as an appropriate promoter or control sequence, may be employed to transform an appropriate host to permit the host to express the protein. Examples of appropriate expression hosts include: bacterial cells, such as *E.coli, Streptomyces, Salmonella typhimurium*; fungal cells, such as yeast; insect cells such as *Drosophila* and *Spodoptera* Sf9; animal cells such as CHO, COS, HEK 293 or Bowes melanoma; adenoviruses; plant cells, etc. The selection of an appropriate host is deemed to be within the scope of those skilled in the art from the teachings herein. The invention is not limited by the host cells employed.

In bacterial systems, a number of expression vectors may be selected depending upon the use intended for the variant product. For example, when

large quantities of variant product are needed for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be desirable. Such vectors include, but are not limited to, multifunctional *E.coli* cloning and expression vectors such as *Bluescript*(R) (Stratagene), in which the variant polypeptide coding sequence may be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of beta-galactosidase so that a hybrid protein is produced; *pIN* vectors (Van Heeke & Schuster *J. Biol. Chem.* **264**:5503-5509, (1989)); *pET* vectors (Novagen, Madison WI); and the like.

In the yeast *Saccharomyces cerevisiae* a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase and PGH may be used. For reviews, see Ausubel *et al. (supra)* and Grant *et al.*, (*Methods in Enzymology* **153**:516-544, (1987)).

In cases where plant expression vectors are used, the expression of a sequence encoding variant product may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of *CaMV* (Brisson *et al., Nature* **310**:511-514. (1984)) may be used alone or in combination with the omega leader sequence from TMV (Takamatsu *et al.*, *EMBO J.*, **6**:307-311, (1987)). Alternatively, plant promoters such as the small subunit of RUBISCO (Coruzzi *et al.*, *EMBO J.* **3**:1671-1680, (1984); Broglie *et al.*, *Science* **224**:838-843, (1984)); or heat shock promoters (Winter J and Sinibaldi R.M., *Results Probl. Cell Differ.*, **17**:85-105, (1991)) may be used. These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. For reviews of such techniques, see Hobbs S. or Murry L.E. (1992) in McGraw Hill Yearbook of Science and Technology, McGraw Hill, New York, N.Y., pp 191-196; or Weissbach and Weissbach (1988) *Methods for Plant Molecular Biology*, Academic Press, New York, N.Y., pp 421-463.

Variant product may also be expressed in an insect system. In one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a

vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The variant product coding sequence may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of variant coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which variant protein is expressed (Smith *et al., J. Virol.* 46:584, (1983); Engelhard, E.K. *et al., Proc. Nat. Acad. Sci.* **91**:3224-7, (1994)).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, a variant product coding sequence may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a nonessential E1 or E3 region of the viral genome will result in a viable virus capable of expressing variant protein in infected host cells (Logan and Shenk, *Proc. Natl. Acad. Sci.* **81**:3655-59, (1984). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be required for efficient translation of a variant product coding sequence. These signals include the ATG initiation codon and adjacent sequences. In cases where variant product coding sequence, its initiation codon and upstream sequences are inserted into the appropriate expression vector, no additional translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous transcriptional control signals including the ATG initiation codon must be provided. Furthermore, the initiation codon must be in the correct reading frame to ensure transcription of the entire insert. Exogenous transcriptional elements and initiation codons can be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate to the cell system in use (Scharf, D. *et al.,*

(1994) *Results Probl. Cell Differ.*, **20**:125-62, (1994); Bittner et al., *Methods in Enzymol* **153**:516-544, (1987)).

In a further embodiment, the present invention relates to host cells containing the above-described constructs. The host cell can be a higher eukaryotic cell, such as a mammalian cell, or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-Dextran mediated transfection, or electroporation (Davis, L., Dibner, M., and Battey, I. (1986) Basic Methods in Molecular Biology). Cell-free translation systems can also be employed to produce polypeptides using RNAs derived from the DNA constructs of the present invention.

A host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the protein include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation. Post-translational processing which cleaves a *"pre-pro"* form of the protein may also be important for correct insertion, folding and/or function. Different host cells such as CHO, HeLa, MDCK, 293, WI38, etc. have specific cellular machinery and characteristic mechanisms for such post-translational activities and may be chosen to ensure the correct modification and processing of the introduced, foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express variant product may be transformed using expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which successfully express the

introduced sequences. Resistant clumps of stably transformed cells can be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler M., *et al.*, *Cell* **11**:223-32, (1977)) and adenine phosphoribosyltransferase (Lowy I., *et al.*, *Cell* **22**:817-23, (1980)) genes which can be employed in *tk-* or *aprt-* cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, *dhfr* which confers resistance to methotrexate (Wigler M., *et al., Proc. Natl. Acad. Sci.* 77:3567-70, (1980)); *npt*, which confers resistance to the aminoglycosides neomycin and G-418 (Colbere-Garapin, F. *et al., J. Mol. Biol.*, **150**:1-14, (1981)) and *als* or *pat*, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, *trpB*, which allows cells to utilize indole in place of tryptophan, or *hisD*, which allows cells to utilize histinol in place of histidine (Hartman S.C. and R.C. Mulligan, *Proc. Natl. Acad. Sci.* **85**:8047-51, (1988)). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate, GUS, and luciferase and its substrates, luciferin and ATP, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C.A. *et. al., Methods Mol. Biol.*, 55:121-131, (1995)).

Host cells transformed with a nucleotide sequence encoding variant product may be cultured under conditions suitable for the expression and recovery of the encoded protein from cell culture. The product produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing nucleic acid sequences encoding variant product can be designed with signal sequences which direct secretion of variant product through a prokaryotic or eukaryotic cell membrane.

The variant product may also be expressed as a recombinant protein with one or more additional polypeptide domains added to facilitate protein purification. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp, Seattle, Wash.). The inclusion of a protease-cleavable polypeptide linker sequence between the purification domain and variant product is useful to facilitate purification. One such expression vector provides for expression of a fusion protein compromising a variant polypeptide fused to a polyhistidine region separated by an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography, as described in Porath, *et al.*, *Protein Expression and Purification,* **3**:263-281, (1992)) while the enterokinase cleavage site provides a means for isolating variant polypeptide from the fusion protein. *pGEX* vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to ligand-agarose beads (e.g., glutathione-agarose in the case of GST-fusions) followed by elution in the presence of free ligand.

Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents, or other methods, which are well know to those skilled in the art.

The variant products can be recovered and purified from recombinant cell cultures by any of a number of methods well known in the art, including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography, and lectin chromatography. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps.

C. Diagnostic applications utilizing nucleic acid sequences

The nucleic acid sequences of the present invention may be used for a variety of diagnostic purposes. The nucleic acid sequences may be used to detect and quantitate expression of the variant in patient's cells, e.g. biopsied tissues, by detecting the presence of mRNA coding for variant product. Alternatively, the assay may be used to detect soluble variant in the serum or blood. This assay typically involves obtaining total mRNA from the tissue or serum and contacting the mRNA with a nucleic acid probe. The probe is a nucleic acid molecule of at least 20 nucleotides, preferably 20-30 nucleotides, capable of specifically hybridizing with a sequence included within the sequence of a nucleic acid molecule encoding variant product under hybridizing conditions, detecting the presence of mRNA hybridized to the probe, and thereby detecting the expression of variant. This assay can be used to distinguish between absence, presence, and excess expression of variant product and to monitor levels of variant expression during therapeutic intervention. In addition, the assay may be used to compare the levels of the variant of the invention to the levels of the original sequence from which it has been varied or to levels of other variants, which comparison may have some physiological meaning.

The invention also contemplates the use of the nucleic acid sequences as a diagnostic for diseases resulting from inherited defective variant sequences, or

diseases in which the ratio of the amount of the original sequence from which the variant was varied to the novel variants of the invention is altered. These sequences can be detected by comparing the sequences of the defective (i.e., mutant) variant coding region with that of a normal coding region. Association of the sequence coding for mutant variant product with abnormal variant product activity may be verified. In addition, sequences encoding mutant variant products can be inserted into a suitable vector for expression in a functional assay system (e.g., colorimetric assay, complementation experiments in a variant protein deficient strain of HEK293 cells) as yet another means to verify or identify mutations. Once mutant genes have been identified, one can then screen populations of interest for carriers of the mutant gene.

Individuals carrying mutations in the nucleic acid sequence of the present invention may be detected at the DNA level by a variety of techniques. Nucleic acids used for diagnosis may be obtained from a patient's cells, including but not limited to such as from blood, urine, saliva, placenta, tissue biopsy and autopsy material. Genomic DNA may be used directly for detection or may be amplified enzymatically by using PCR (Saiki, *et al.*, *Nature* **324**:163-166, (1986)) prior to analysis. RNA or cDNA may also be used for the same purpose. As an example, PCR primers complementary to the nucleic acid of the present invention can be used to identify and analyze mutations in the gene of the present invention. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype.

Point mutations can be identified by hybridizing amplified DNA to radiolabeled RNA of the invention or alternatively, radiolabeled antisense DNA sequences of the invention. Sequence changes at specific locations may also be revealed by nuclease protection assays, such RNase and S1 protection or the chemical cleavage method (e.g. Cotton, *et alProc. Natl. Acad. Sci.* USA, **85**:4397-4401, (1985)), or by differences in melting temperatures. *"Molecular beacons"* (Kostrikis L.G. *et al.*, Science **279**:1228-1229, (1998)), hairpin-shaped, single-stranded synthetic oligonucleotides containing probe sequences which are

complementary to the nucleic acid of the present invention, may also be used to detect point mutations or other sequence changes as well as monitor expression levels of variant product. Such diagnostics would be particularly useful for prenatal testing.

Another method for detecting mutations uses two DNA probes which are designed to hybridize to adjacent regions of a target, with abutting bases, where the region of known or suspected mutation(s) is at or near the abutting bases. The two probes may be joined at the abutting bases, e.g., in the presence of a ligase enzyme, but only if both probes are correctly base paired in the region of probe junction. The presence or absence of mutations is then detectable by the presence or absence of ligated probe.

Also suitable for detecting mutations in the variant product coding sequence are oligonucleotide array methods based on sequencing by hybridization (SBH), as described, for example, in U.S. Patent No. 5,547,839. In a typical method, the DNA target analyte is hybridized with an array of oligonucleotides formed on a microchip. The sequence of the target can then be "read" from the pattern of target binding to the array.

D. Gene mapping utilizing nucleic acid sequences

The nucleic acid sequences of the present invention are also valuable for chromosome identification. The sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome. Moreover, there is a current need for identifying particular sites on the chromosome. Few chromosome marking reagents based on actual sequence data (repeat polymorphisms) are presently available for marking chromosomal location. The mapping of DNAs to chromosomes according to the present invention is an important first step in correlating those sequences with genes associated with disease.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 20-30 bp) from the variant cDNA. Computer analysis of the

3' untranslated region is used to rapidly select primers that do not span more than one exon in the genomic DNA, which would complicate the amplification process. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the primer will yield an amplified fragment.

PCR mapping of somatic cell hybrids or using instead radiation hybrids are rapid procedures for assigning a particular DNA to a particular chromosome. Using the present invention with the same oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes or pools of large genomic clones in an analogous manner. Other mapping strategies that can similarly be used to map to its chromosome include *in situ* hybridization, prescreening with labeled flow-sorted chromosomes and preselection by hybridization to construct chromosome specific-cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a cDNA clone to a metaphase chromosomal spread can be used to provide a precise chromosomal location in one step. This technique can be used with cDNA as short as 50 or 60 bases. For a review of this technique, see Verma *et al., Human Chromosomes: a Manual of Basic Techniques*, (1988) Pergamon Press, New York.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, for example, in the OMIM database (Center for Medical Genetics, Johns Hopkins University, Baltimore, MD and National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD). The OMIM gene map presents the cytogenetic map location of disease genes and other expressed genes. The OMIM database provides information on diseases associated with the chromosomal location. Such associations include the results of linkage analysis mapped to this interval, and the correlation of translocations and other chromosomal aberrations in this area with the advent of polygenic diseases, such as cancer, in general and prostate cancer in particular.

E. Therapeutic applications of nucleic acid sequences

Nucleic acid sequences of the invention may also be used for therapeutic purposes. Turning first to the second aspect of the invention (i.e. inhibition of expression of variant), expression of variant product may be modulated through antisense technology, which controls gene expression through hybridization of complementary nucleic acid sequences, i.e. antisense DNA or RNA, to the control, 5' or regulatory regions of the gene encoding variant product. For example, the 5' coding portion of the nucleic acid sequence sequence which codes for the product of the present invention is used to design an antisense oligonucleotide of from about 10 to 40 base pairs in length. Oligonucleotides derived from the transcription start site, e.g. between positions -10 and +10 from the start site, are preferred. An antisense DNA oligonucleotide is designed to be complementary to a region of the nucleic acid sequence involved in transcription (Lee *et al., Nucl. Acids, Res.*, **6**:3073, (1979); Cooney et al., Science **241**:456, (1988); and Dervan *et al., Science* **251**:1360, (1991)), thereby preventing transcription and the production of the variant products. An antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into the variant products (Okano *J. Neurochem.* **56**:560, (1991)). The antisense constructs can be delivered to cells by procedures known in the art such that the antisense RNA or DNA may be expressed *in vivo*. The antisense may be antisense mRNA or DNA sequence capable of coding such antisense mRNA. The antisense mRNA or the DNA coding thereof can be complementary to the full sequence of nucleic acid sequences coding for the variant protein or to a fragment of such a sequence which is sufficient to inhibit production of a protein product.

Turning now to the first aspect of the invention, i.e. expression of variant, expression of variant product may be increased by providing coding sequences for coding for said product under the control of suitable control elements ending its expression in the desired host.

The nucleic acid sequences of the invention may be employed in combination with a suitable pharmaceutical carrier. Such compositions comprise a therapeutically effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier includes but is not limited to saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The formulation should suit the mode of administration.

The products of the invention as well as any activators and deactivators compounds (see below) which are polypeptides, may also be employed in accordance with the present invention by expression of such polypeptides *in vivo*, which is often referred to as *"gene therapy."* Cells from a patient may be engineered with a nucleic acid sequence (DNA or RNA) encoding a polypeptide *ex vivo*, with the engineered cells then being provided to a patient to be treated with the polypeptide. Such methods are well-known in the art. For example, cells may be engineered by procedures known in the art by use of a retroviral particle containing RNA encoding a polypeptide of the present invention.

Similarly, cells may be engineered in vivo for expression of a polypeptide *in vivo* by procedures known in the art. As known in the art, a producer cell for producing a retroviral particle containing RNA encoding the polypeptide of the present invention may be administered to a patient for engineering cells *in vivo* and expression of the polypeptide *in vivo*. These and other methods for administering a product of the present invention by such method should be apparent to those skilled in the art from the teachings of the present invention. For example, the expression vehicle for engineering cells may be other than a retrovirus, for example, an adenovirus which may be used to engineer cells *in vivo* after combination with a suitable delivery vehicle.

Retroviruses from which the retroviral plasmid vectors mentioned above may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, retroviruses such as Rous Sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, adenovirus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the *PE501*, *PA317*, *psi-2*, *psi-AM*, *PA12*, *T19-14X*, *VT-19-17-H2*, *psi-CRE*, *psi-CRIP*, *GP+E-86*, *GP+envAm12*, and *DAN* cell lines as described in Miller (*Human Gene Therapy*, Vol. **1**, pg. 5-14, (1990)). The vector may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and $CaPO_4$ precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include the nucleic acid sequence(s) encoding the polypeptides. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either *in vitro* or *in vivo*. The transduced eukaryotic cells will express the nucleic acid sequence(s) encoding the polypeptide. Eukaryotic cells which may be transduced include, but are not limited to, embryonic stem cells, embryonic carcinoma cells, as well as hematopoietic stem cells, hepatocytes, fibroblasts, myoblasts, keratinocytes, endothelial cells, and bronchial epithelial cells.

The genes introduced into cells may be placed under the control of inducible promoters, such as the radiation-inducible Egr-1 promoter, (Maceri, H.J., *et al., Cancer Res.*, **56**(19):4311 (1996)), to stimulate variant production or antisense inhibition in response to radiation, eg., radiation therapy for treating tumors.

Example III. Variant product

The substantially purified variant product of the invention has been defined above as the product coded from the nucleic acid sequence of the invention. Preferably the amino acid sequence is an amino acid sequence having at least 90% identity to any one of the sequences identified as SEQ ID NO: 37 to SEQ ID NO: 72 provided that the amino acid sequence is not identical to that of

the original sequence from which it has been varied. The protein or polypeptide may be in mature and/or modified form, also as defined above. Also contemplated are protein fragments having at least 10 contiguous amino acid residues, preferably at least 10-20 residues, derived from the variant product, as well as homologues as explained above.

The sequence variations are preferably those that are considered conserved substitutions, as defined above. Thus, for example, a protein with a sequence having at least 90% sequence identity with any of the products identified as SEQ ID NO: 37 to SEQ ID NO: 72, preferably by utilizing conserved substitutions as defined above is also part of the invention, and provided that it is not identical to the original peptide from which it has been varied. In a more specific embodiment, the protein has or contains any one of the sequence identified as SEQ ID NO: 37 to SEQ ID NO: 72. The variant product may be (i) one in which one or more of the amino acid residues in a sequence listed above are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue), or (ii) one in which one or more of the amino acid residues includes a substituent group, or (iii) one in which the variant product is fused with another compound, such as a compound to increase the half-life of the protein (for example, polyethylene glycol (PEG)), or a moiety which serves as targeting means to direct the protein to its target tissue or target cell population (such as an antibody), or (iv) one in which additional amino acids are fused to the variant product. Such fragments, variants and derivatives are deemed to be within the scope of those skilled in the art from the teachings herein.

A. Preparation of variant product

Recombinant methods for producing and isolating the variant product, and fragments of the protein are described above.

In addition to recombinant production, fragments and portions of variant product may be produced by direct peptide synthesis using solid-phase techniques (cf. Stewart *et al.*, (1969) Solid-Phase Peptide Synthesis, WH Freeman Co, San

Francisco; Merrifield J., *J. Am. Chem. Soc.*, **85**:2149-2154, (1963)). In vitro peptide synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer, Foster City, Calif.) in accordance with the instructions provided by the manufacturer. Fragments of variant product may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

II. Therapeutic uses and compositions utilizing the variant product

The variant product of the invention is generally useful in treating diseases and disorders which are characterized by a lower than normal level of variant expression, and or diseases which can be cured or ameliorated by raising the level of the variant product, even if the level is normal.

Variant products or fragments may be administered by any of a number of routes and methods designed to provide a consistent and predictable concentration of compound at the target organ or tissue. The product-containing compositions may be administered alone or in combination with other agents, such as stabilizing compounds, and/or in combination with other pharmaceutical agents such as drugs or hormones.

Variant product-containing compositions may be administered by a number of routes including, but not limited to oral, intravenous, intramuscular, transdermal, subcutaneous, topical, sublingual, or rectal means as well as by nasal application. Variant product-containing compositions may also be administered via liposomes. Such administration routes and appropriate formulations are generally known to those of skill in the art.

The product can be given via intravenous or intraperitoneal injection. Similarly, the product may be injected to other localized regions of the body. The product may also be administered via nasal insufflation. Enteral administration is also possible. For such administration, the product should be formulated into an

appropriate capsule or elixir for oral administration, or into a suppository for rectal administration.

The foregoing exemplary administration modes will likely require that the product be formulated into an appropriate carrier, including ointments, gels, suppositories. Appropriate formulations are well known to persons skilled in the art.

Dosage of the product will vary, depending upon the potency and therapeutic index of the particular polypeptide selected.

A therapeutic composition for use in the treatment method can include the product in a sterile injectable solution, the polypeptide in an oral delivery vehicle, the product in an aerosol suitable for nasal administration, or the product in a nebulized form, all prepared according to well known methods. Such compositions comprise a therapeutically effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier includes but is not limited to saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The product of the invention may also be used to modulate endothelial differentiation and proliferation as well as to modulate apoptosis either *ex vivo* or *in vitro*, for example, in cell cultures.

Example IV. Screening methods for activators and deactivators (inhibitors)

The present invention also includes an assay for identifying molecules, such as synthetic drugs, antibodies, peptides, or other molecules, which have a modulating effect on the activity of the variant product, e.g. activators or deactivators of the variant product of the present invention. Such an assay comprises the steps of providing an variant product encoded by the nucleic acid sequences of the present invention, contacting the variant protein with one or more candidate molecules to determine the candidate molecules modulating effect on the activity of the variant product, and selecting from the molecules a candidate's molecule capable of modulating variant product physiological activity.

The variant product, its catalytic or immunogenic fragments or oligopeptides thereof, can be used for screening therapeutic compounds in any of a variety of drug screening techniques. The fragment employed in such a test may be free in solution, affixed to a solid support, borne on a cell membrane or located intracellularly. The formation of binding complexes, between variant product and the agent being tested, may be measured. Alternatively, the activator or deactivator may work by serving as agonist or antagonist, respectively, of the variant receptor, binding entity or target site, and their effect may be determined in connection with any of the above.

Another technique for drug screening which may be used provides for high throughput screening of compounds having suitable binding affinity to the variant product is described in detail by Geysen in PCT Application WO 84/03564, published on Sep. 13, 1984. In summary, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with the full variant product or with fragments of variant product and washed. Bound variant product is then detected by methods well known in the art. Substantially purified variant product can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

Antibodies to the variant product, as described in Example VI below, may also be used in screening assays according to methods well known in the art. For example, a *"sandwich"* assay may be performed, in which an anti-variant antibody is affixed to a solid surface such as a microtiter plate and variant product is added. Such an assay can be used to capture compounds which bind to the variant product. Alternatively, such an assay may be used to measure the ability of compounds to influence with the binding of variant product to the variant receptor, and then select those compounds which effect the binding.

Example V. Anti-variant antibodies

A. Synthesis

In still another aspect of the invention, the purified variant product is used to produce anti-variant antibodies which have diagnostic and therapeutic uses related to the activity, distribution, and expression of the variant product.

Antibodies to the variant product may be generated by methods well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, humanized, single chain, Fab fragments and fragments produced by an Fab expression library. Antibodies, i.e., those which inhibit dimer formation, are especially preferred for therapeutic use.

A fragment of the variant product for antibody induction does not require biological activity but have to feature immunological activity; however, the protein fragment or oligopeptide must be antigenic. Peptides used to induce specific antibodies may have an amino acid sequence consisting of at least five amino acids, preferably at least 10 amino acids of the sequences specified in any one of SEQ ID NO: 37 to SEQ ID NO: 72. Preferably they should mimic a portion of the amino acid sequence of the natural protein and may contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of variant protein amino acids may be fused with those of another protein such as keyhole limpet hemocyanin and antibody produced against the chimeric molecule. Procedures well known in the art can be used for the production of antibodies to variant product.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, etc may be immunized by injection with variant product or any portion, fragment or oligopeptide which retains immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include but are not limited to Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet

hemocyanin, and dinitrophenol. BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are potentially useful human adjuvants.

Monoclonal antibodies to variant protein may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include but are not limited to the hybridoma technique originally described by Koehler and Milstein (*Nature* **256**:495-497, (1975)), the human B-cell hybridoma technique (Kosbor *et al., Immunol. Today* **4**:72, (1983); Cote *et al., Proc. Natl. Acad. Sci.* **80**:2026-2030, (1983)) and the EBV-hybridoma technique (Cole, *et al., Mol. Cell Biol.* 62:109-120, (1984)).

Techniques developed for the production of *"chimeric antibodies"*, the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity can also be used (Morrison *et al., Proc. Natl. Acad. Sci.* **81**:6851-6855, (1984); Neuberger *et al., Nature* **312**:604-608, (1984); Takeda *et al., Nature* **314**:452-454, (1985)). Alternatively, techniques described for the production of single chain antibodies (U.S. Pat. No. 4,946,778) can be adapted to produce single-chain antibodies specific for the variant protein.

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening recombinant immunoglobulin libraries or panels of highly specific binding reagents as disclosed in Orlandi *et al.* (*Proc. Natl. Acad. Sci.* **86**:3833-3837, 1989)), and Winter G and Milstein C., (*Nature* **349**:293-299, (1991)).

Antibody fragments which contain specific binding sites for variant protein may also be generated. For example, such fragments include, but are not limited to, the $F(ab')_2$ fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the $F(ab')_2$ fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity (Huse W.D. *et al., Science* 256:1275-1281, (1989)).

B. Diagnostic applications of antibodies

A variety of protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the formation of complexes between the variant product and its specific antibody and the measurement of complex formation. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two noninterfering epitopes on a specific variant product is preferred, but a competitive binding assay may also be employed. These assays are described in Maddox D.E., *et al.*, (*J. Exp. Med.* **158**:1211, (1983)).

Antibodies which specifically bind variant product are useful for the diagnosis of conditions or diseases characterized by expression of the novel variant of the invention (where normally it is not expressed) by over or under expression of variant as well as for detection of diseases in which the proportion between the amount of the variants of the invention and the original sequence from which it varied is altered. Alternatively, such antibodies may be used in assays to monitor patients being treated with variant product, its activators, or its deactivators. Diagnostic assays for variant protein include methods utilizing the antibody and a label to detect variant product in human body fluids or extracts of cells or tissues. The products and antibodies of the present invention may be used with or without modification. Frequently, the proteins and antibodies will be labeled by joining them, either covalently or noncovalently, with a reporter molecule. A wide variety of reporter molecules are known in the art.

A variety of protocols for measuring the variant product, using either polyclonal or monoclonal antibodies specific for the respective protein are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescent activated cell sorting (FACS). As noted above, a two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on variant product is

preferred, but a competitive binding assay may be employed. These assays are described, among other places, in Maddox, *et al. (supra)*. Such protocols provide a basis for diagnosing altered or abnormal levels of variant product expression. Normal or standard values for variant product expression are established by combining body fluids or cell extracts taken from normal subjects, preferably human, with antibody to variant product under conditions suitable for complex formation which are well known in the art. The amount of standard complex formation may be quantified by various methods, preferably by photometric methods. Then, standard values obtained from normal samples may be compared with values obtained from samples from subjects potentially affected by disease. Deviation between standard and subject values establishes the presence of disease state.

The antibody assays are useful to determine the level of variant product present in a body fluid sample, in order to determine whether it is being expressed at all, whether it is being overexpressed or underexpressed in the tissue, or as an indication of how variant levels of variable products are responding to drug treatment.

By another aspect the invention concerns methods for determining the presence or level of various anti-variant antibodies in a biological sample obtained from patients, such as blood or serum sample using as an antigen the variant product. Determination of said antibodies may be indicative to a plurality of pathological conditions or diseases.

C. Therapeutic uses of antibodies

In addition to their diagnostic use the antibodies may have a therapeutical utility in blocking or decreasing the activity of the variant product in pathological conditions where beneficial effect can be achieved by such a decrease.

The antibody employed is preferably a humanized monoclonal antibody, or a human Mab produced by known globulin-gene library methods. The antibody is administered typically as a sterile solution by IV injection, although

other parenteral routes may be suitable. Typically, the antibody is administered in an amount between about 1-15 mg/kg body weight of the subject. Treatment is continued, e.g., with dosing every 1-7 days, until a therapeutic improvement is seen.

Although the invention has been described with reference to specific methods and embodiments, it is appreciated that various modifications and changes may be made without departing from the invention.

CLAIMS:

1. An isolated nucleic acid sequence, of an alternative splicing variant, selected from the group consisting of:

(i) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 36;

(ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and

(iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.

2. An isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 1.

3. An amino acid sequence selected from the group consisting of:

(i) an amino acid sequence coded by the isolated nucleic acid sequence of alternative splice variants of Claim 1;

(ɔ) homologues of the amino acid sequences of (i) in which one or more amino acids has been added, deleted, replaced or chemically modified in the region or adjacent to the region where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied.

4. An amino acid sequence according to Claim 3, as depicted in any one of SEQ ID NO: 37 to SEQ ID NO: 72.

5. An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 3 or 4.

6. A purified antibody which binds specifically to any of the amino acid sequence of Claim 3 or 4.

7. An expression vector comprising any one of the nucleic acid sequences of Claim 1 or 5 and control elements for the expression of the nucleic acid sequence in a suitable host.

8. An expression vector comprising any one of the nucleic acid sequences of Claim 2, and control elements for the expression of the nucleic acid sequences in a suitable host.

9. A host cell transfected by the expression vector of Claim 7 or 8.

10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

(i) the expression vector of Claim 7; and

(ii) any one of the amino acid sequences of Claim 3 or 4.

11. A pharmaceutical composition according to Claim 10, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO: 37 to SEQ ID NO: 72.

12. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

(i) any one of the nucleic acid sequences of Claim 2;

(ii) the expression vector of Claim 8; and

(iii) the purified antibody of Claim 6.

13. A pharmaceutical composition according to Claim 12, for treatment of diseases which can be ameliorated or cured by decreasing the level of any one of the amino acid sequences depicted in SEQ ID NO: 37 to SEQ ID NO: 72.

14. A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and

(b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

15. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

16. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

(i) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 15;

(ii) determining the level of the original sequence in the second biological sample; and

(iii) comprising the levels obtained in (a) and (b) to give said ratio.

17. A method according to Claim 16, wherein said first and said second biological samples are the same sample.

18. A method according to any of Claims 14 to 17, wherein the nucleic acid material of said biological sample are mRNA transcripts.

19. A method according to Claim 18, where the nucleic acid sequence is present in a nucleic acid chip.

20. A method for identifying candidate compounds capable of binding to the variant product and modulating its activity the method comprising:

(i) providing any one of the amino acid sequences as defined in Claim 3 or 4;

(ii) contacting a candidate compound with said amino acid sequence;

(iii) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.

21. A method according to Claim 20, wherein the compound is an activator and the measured effect is increase in the biological activity.

22. A method according to Claim 20, wherein the compound is an deactivator and the effect is decrease in the biological activity.

23. An activator of any one of the amino acid sequences of Claim 3 or 4.

24. An deactivator of any one of the amino acid sequences of Claims 3 or 4.

25. A method for detecting any one of the amino acid sequences of Claim 3 or 4 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of Claim 8, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

26. A method for detecting the level of the amino acid sequence of any one of Claim 3 or 4 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of Claim 8, thereby forming an antibody-antigen complex; and

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

27. A method for determining the ratio between the level of any one of the amino acid sequences of Claims 3 or 4 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

(i) determining the level of the amino acid sequences of Claims 3 or 4 into a first sample by the method of Claim 26;

(ii) determining the level of the original amino acid sequence in the second sample; and

(iii) comparing the level obtained in (a) and (b) to give said ratio.

28. A method according to Claim 27, wherein said first and said second biological samples are the same sample.

29. A method for detecting any one of the antibodies of Claim 6 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 3 or 4 thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the antibody in said biological sample.

30. A method for detecting the level of any one of the antibodies of Claim 6 in a biological sample comprising the steps of:

(i) contacting said biological sample with any one of the amino acid sequences of Claim 3;

(ii) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the levels of said antibody in the sample.

For the Applicants,
REINHOLD COHN AND PARTNERS
By:

SEQUENCE LISTING

<110> COMPUGEN LTD.

<120> SPLICE VARIANTS OF ONCOGENES

<130> 1245448-COMPUGEN

<140>
<141>

<160> 72

<170> PatentIn Ver. 2.1

<210> 1
<211> 1735
<212> DNA
<213> Homo sapiens

<400> 1
gtccaccgga agcgagttgc gacacggcag gttcccgccc ggaagaagcg accaaagcgc 60
ctgaggaccg gcaacatggt gcggtcgggg aataaggcag ctgttgtgct gtgtatggac 120
gtgggcttta ccatgagtaa ctccattcct ggtatagaat ccccatttga acaagcaaag 180
aaggtgataa ccatgtttgt acagcgacag gtgtttgctg agaacaagga tgagattgct 240
ttagtcctgt ttggtacaga tggcactgac aatccccttt ctggtgggga tcagtatcag 300
aacatcacag tgcacagaca tctgatgcta ccagattttg atttgctgga ggacattgaa 360
agcaaaatcc aaccaggttc tcaacaggct gacttcctgg atgcactaat cgtgagcatg 420
gatgtgattc aacatgaaac aataggaaag aagtttgaga agaggcatat tgaaatattc 480
actgacctca gcagccgatt cagcaaaagt cagctggata ttataattca tagcttgaag 540
aaatgtgaca tctccctgca attcttcttg cctttctcac ttggcaagga agatggaagt 600
ggggacagag gagatggccc ctttcgctta ggtggccatg ggccttcctt tccactaaaa 660
ggaattaccg aacagcaaaa agaaggtctt gagatagtga aaatggtgat gatatcttta 720
gaaggtgaag atgggttgga tgaaatttat tcattcagtg agagtctgag aaaactgtgc 780
gtcttcaaga aaattgagag gcattccatt cactggccct gccgactgac cattggctcc 840
aatttgtcta taaggattgc agcctataaa tcgattctac aggagagagt taaaaagact 900
tggacagttg tggatgcaaa aaccctaaaa aaagaagata tacaaaaaga aacagtttat 960
tgcttaaatg atgatgatga aactgaagtt ttaaaagagg atattattca agggttccgc 1020
tatggaagtg atatagttcc tttctctaaa gtggatgagg aacaaatgaa atataaatcg 1080
gaggggaagt gcttctctgt tttgggattt tgtaaatctt ctcaggttca gagaagattc 1140
ttcatgggaa atcaagttct aaaggtcttt gcagcaagag atgatgaggc agctgcagtt 1200
gcactttcct ccctgattca tgctttggat gacttagaca tggtggccat agttcgatat 1260
gcttatgaca aaagagctaa tcctcaagtc ggcgtggctt ttcctcatat caagcataac 1320
tatgagtgtt tagtgtatgt gcagctgcct ttcatggaag acttgcggca atacatgttt 1380
tcatccttga aaaacagtaa gaaatatgct cccaccgagg cacagttgaa tgctgttgat 1440
gctttgattg actccatgag cttggcaaag aaagatgaga agacagacac ccttgaagac 1500
ttgtttccaa ccaccaaaat cccaaatcct cgatttcaga gattatttca ggtaagagaa 1560
gaaggatgaa caagtcatat ttcttttaaa tgaaagagag ctaagtgcaa agttgcggta 1620
attggccagt cctaaataaa tgtcttttt ctctgaaggc cccatttgct ctatttaatg 1680
gaagaataac atcttcctct cctacttcag aaggtaaaaa tattctgagc tctta 1735

<210> 2
<211> 2766
<212> DNA
<213> Homo sapiens

<400> 2
gtccaccgga agcgagttgc gacacggcag gttcccgccc ggaagaagcg accaaagcgc 60
ctgaggaccg gcaacatggt gcggtcgggg aataaggcag ctgttgtgct gtgtatggac 120
gtgggcttta ccatgagtaa ctccattcct ggtatagaat ccccatttga acaagcaaag 180

aaggtgataa ccatgtttgt acagcgacag gtgtttgctg agaacaagga tgagattgct 240
ttagtcctgt ttggtacaga tggcactgac aatccccttt ctggtgggga tcagtatcag 300
aacatcacag tgcacagaca tctgatgcta ccagattttg atttgctgga ggacattgaa 360
agcaaaatcc aaccaggttc tcaacaggct gacttcctgg atgcactaat cgtgagcatg 420
gatgtgattc aacatgaaac aataggaaag aagtttgaga agaggcatat tgaaatattc 480
actgacctca gcagccgatt cagcaaaagt cagctggata ttataattca tagcttgaag 540
aaatgtgaca tctccctgca attcttcttg cctttctcac ttggcaagga agatggaagt 600
ggggacagag gagatggccc ctttcgctta ggtggccatg ggccttcctt tccactaaaa 660
ggaattaccg aacagcaaaa agaaggtctt gagatagtga aaatggtgat gatatcttta 720
gaaggtgaag atgggttgga tgaaatttat tcattcagtg agagtctgag aaaactgtgc 780
gtcttcaaga aaattgagag gcattccatt cactggccct gccgactgac cattggctcc 840
aatttgtcta taaggattgc agcctataaa tcgattctac aggagagagt taaaaagact 900
tggacagttg tggatgcaaa aaccctaaaa aaagaagata tacaaaaaga aacagtttat 960
tgcttaaatg atgatgatga aactgaactg aatcctcccg ctgaggtgac aacgaaaagt 1020
cagattcctc tctctaaaat aaagaccctt tttcctctga ttgaagccaa gaaaaaggat 1080
caagtgactg ctcaggaaat tttccaagac aaccatgaag atggacctac agctaaaaaa 1140
ttaaagactg agcaaggggg agcccacttc agcgtctcca gtctggctga aggcagtgtc 1200
acctctgttg gaagtgtgaa tcctgctgaa aacttccgtg ttctagtgaa acagaagaag 1260
gccagctttg aggaagcgag taaccagctc ataaatcaca tcgaacagtt tttggatact 1320
aatgaaacac cgtattttat gaagagcata gactgcatcc gagccttccg ggaagaagcc 1380
attaagtttt cagaagagca gcgctttaac aacttcctga aagcccttca agagaaagtg 1440
gaaattaaac aattaaatca tttctgggaa attgttgtcc aggatggaat tactctgatc 1500
accaaagagg aagcctctgg aagttctgtc acagctgagg aagccaaaaa gtttctggcc 1560
cccaaagaca aaccaagtgg agacacagca gctgtatttg aagaaggtgg tgatgtggac 1620
gatttattgg acatgatata ggtcgtggat gtatggggaa tctaagagag ctgccatcgc 1680
tgtgatgctg ggagttctaa caaaacaagt tggatgcggc cattcaaggg gagccaaaat 1740
ctcaagaaat tcccagcagg ttacctggag gcggatcatc taattctctg tggaatgaat 1800
acacacatat atattacaag ggataattta gaccccatac aagtttataa agagtcattg 1860
ttattttctg gttggtgtat tatttttttct gtggtcttac tgatctttgt atattacata 1920
catgctttga agtttctgga aagtagatct tttcttgacc tagtatatca gtgacagttg 1980
cagcccttgt gatgtgatta gtgtctcatg tggaaccatg gcatggttat tgatgagttt 2040
cttaaccctt tccagagtcc tcctttgcct gatcctccaa cagctgtcac aacttgtgtt 2100
gagcaagcag tagcatttgc ttcctcccaa caagcagctg ggttaggaaa accatgggta 2160
aggacggact cacttctctt tttagttgag gccttctagt taccacatta ctctgcctct 2220
gtatataggt ggttttcttt aagtggggtg ggaaggggag cacaatttcc cttcatactc 2280
cttttaagca gtgagttatg gtggtggtct catgaagaaa agacctttg gcccaatctc 2340
tgccatatca gtgaaccttt agaaactcaa aaactgagaa atttactaca gtagttagaa 2400
ttatatcact tcactgttct ctacttgcaa gcctcaaaga gagaaagttt cgttatatta 2460
aaacacttag gtaacttttc ggtctttccc atttctacct aagtcagctt tcatctttgt 2520
ggatggtgtc tcctttacta aataagaaaa taacaaagcc cttattctct ttttttcttg 2580
tcctcattct tgccttgagt tccagttcct ctttggtgta cagacttctt ggtacccagt 2640
cacctctgtc ttcagcaccc tcataagtcg tcactaatac acagttttgt acatgtaaca 2700
ttaaaggcat aaatgactca tcaaaaaaaa aaaaaaaaaa aattatggta cctcgaatca 2760
atgtgt 2766

<210> 3
<211> 2034
<212> DNA
<213> Homo sapiens

<400> 3
ggagacaggt ggtggctacg acggcraagg gagctgagac tgtccaggca gccaggttag 60
gccaggagga ccatgtgaat ggggccagag ggctcccggg ctgggcaggg accatgggct 120
gtggctgcag ctcacacccg gaagatgact ggatggaaaa catcgatgtg tgtgagaact 180
gccattatcc catagtccca ctggatggca agggcacgct gctcatccga aatggctctg 240
aggtgcggga cccactggtt acctacgaag gctccaatcc gccggcttcc ccactgcaag 300
acaacctggt tatcgctctg cacagctatg agccctctca cgacggagat ctgggctttg 360
agaaggggga acagctccgc atcctggagc agagcggcga gtggtggaag gcgcagtccc 420
tgaccacggg ccaggaaggc ttcatcccct tcaattttgt ggccaaagcg aacagcctgg 480
agcccgaacc ctggttcttc aagaacctga gccgcaagga cgcggagcgg cagctcctgg 540

cgcccgggaa cactcacggc tccttcctca tccgggagag cgagagcacc gcgggatcgt 600
tttcactgtc ggtccgggac ttcgaccaga accagggaga ggtggtgaaa cattacaaga 660
tccgtaatct ggacaacggt ggcttctaca tctcccctcg aatcactttt cccggcctgc 720
atgaactggt ccgccattac accaatgctt cagatgggct gtgcacacgg ttgagccgcc 780
cctgccagac ccagaagccc cagaagccgt ggtgggagga cgagtgggag gttcccaggg 840
agacgctgaa gctggtggag cggctggggg ctggacagtt cggggaggtg tggatggggt 900
actacaacgg gcacacgaag gtggcggtga agagcctgaa gcagggcagc atgtccccgg 960
acgccttcct ggccgaggcc aacctcatga agcagctgca acaccagcgg ctggttcggc 1020
tctacgctgt ggtcacccag gagcccatct acatcatcac tgaatacatg gagaatggga 1080
gtctagtgga ttttctcaag acccccttcag gcatcaagtt gaccatcaac aaactcctgg 1140
acatggcagc ccaaattgca gaaggcatgg cattcattga agagcggaat tatattcatc 1200
gtgaccttcg ggctgccaac attctggtgt ctgacaccct gagctgcaag attgcagact 1260
ttggcctagc acgcctcatt gaggacattc accatcaagt cagatgtgtg gtcttttggg 1320
atcctgctga cggaaattgt cacccacggc cgcatccctt acccagggat gaccaacccg 1380
gaggtgattc agaacctgga gcgaggctac cgcatggtgc gccctgacaa ctgtccagag 1440
gagctgtacc aactcatgag gctgtgctgg aaggagcgcc cagaggaccg gcccaccttt 1500
gactacctgc gcagtgtgct ggaggacttc ttcacggcca cagagggcca gtaccagcct 1560
cagccttgag aggccttgag aggccctggg gttctccccc tttctctcca gcctgacttg 1620
gggagatgga gttcttgtgc catagtcaca tggcctatgc acatatggac tctgcacatg 1680
aatcccaccc acatgtgaca catatgcacc ttgtgtctgt acacgtgtcc tgtagttgcg 1740
tggactctgc acatgtcttg tacatgtgta gcctgtgcat gtatgtcttg gacactgtac 1800
aaggtacccc tttctggctc tcccatttcc tgagaccaca gagagagggg agaagcctgg 1860
gattgacaga agcttctgcc cacctacttt tctttcctca gatcatccag aagttcctca 1920
agggccagga ctttatctaa tacctctgtg tgctcctcct tggtgcctgg cctggcacac 1980
atcaggagtt caataaatgt ctgttgatga ctgttgtaca caacaacaaa acaa 2034

<210> 4
<211> 2282
<212> DNA
<213> Homo sapiens

<400> 4
ggagacaggt ggtggctacg acggcraagg gagctgagac tgtccaggca gccaggttag 60
gccaggagga ccatgtgaat ggggccagag ggctcccggg ctgggcaggg accatgggct 120
gtggctgcag ctcacacccg gaagatgact ggatggaaaa catcgatgtg tgtgagaact 180
gccattatcc catagtccca ctggatggca agggcacgct gctcatccga aatggctctg 240
aggtgcggga cccactggtt acctacgaag gctccaatcc gccggcttcc ccactgcaag 300
gtgaccccag gcagcagggc ctgaaagaca aggcctgcgg atccctggct gttggcttcc 360
acctctcccc cacctacttt ctccccggtc ttgccttcct tgtcccccac cctgtaactc 420
caggcttcct gccgatccca gctcggttct ccctgacgcc ccttgtcttt acagacaacc 480
tggttatcgc tctgcacagc tatgagccct ctcacgacgg agatctgggc tttgagaagg 540
gggaacagct ccgcatcctg gagcagagcg gcgagtggtg gaaggcgcag tccctgacca 600
cgggccagga aggcttcatc cccttcaatt ttgtggccaa agcgaacagc ctggagcccg 660
aaccctggtt cttcaagaac ctgagccgca aggacgcgga gcggcagctc ctggcgcccg 720
ggaacactca cggctccttc ctcatccggg agagcgagag caccgcggga tcgttttcac 780
tgtcggtccg ggacttcgac cagaaccagg gagaggtggt gaaacattac aagatccgta 840
atctggacaa cggtggcttc tacatctccc ctcgaatcac ttttcccggc ctgcatgaac 900
tggtccgcca ttacaccaat gcttcagatg ggctgtgcac acggttgagc cgcccctgcc 960
agacccagaa gccccagaag ccgtggtggg aggacgagtg ggaggttccc agggagacgc 1020
tgaagctggt ggagcggctg ggggctggac agttcgggga ggtgtggatg gggtactaca 1080
acgggcacac gaaggtggcg gtgaagagcc tgaagcaggg cagcatgtcc ccggacgcct 1140
tcctggccga ggccaacctc atgaagcagc tgcaacacca gcggctggtt cggctctacg 1200
ctgtggtcac ccaggagccc atctacatca tcactgaata catggagaat gggagtctag 1260
tggattttct caagacccct tcaggcatca agttgaccat caacaaactc ctggacatgg 1320
cagcccaaat tgcagaaggc atggcattca ttgaagagcg gaattatatt catcgtgacc 1380
ttcgggctgc caacattctg gtgtctgaca ccctgagctg caagattgca gactttggcc 1440
tagcacgcct cattgaggac aacgagtaca cagccaggga gggggccaag tttcccatta 1500
agtggacagc gccagaagcc attaactacg ggacattcac catcaagtca gatgtgtggt 1560
cttttgggat cctgctgacg gaaattgtca cccacggccg catcccttac ccagggatga 1620
ccaacccgga ggtgattcag aacctggagc gaggctaccg catggtgcgc cctgacaact 1680

gtccagagga gctgtaccaa ctcatgaggc tgtgctggaa ggagcgccca gaggaccggc 1740
ccacctttga ctacctgcgc agtgtgctgg aggacttctt cacggccaca gagggccagt 1800
accagcctca gccttgagag gccttgagag gccctggggt tctccccctt tctctccagc 1860
ctgacttggg gagatggagt tcttgtgcca tagtcacatg gcctatgcac atatggactc 1920
tgcacatgaa tcccacccac atgtgacaca tatgcacctt gtgtctgtac acgtgtcctg 1980
tagttgcgtg gactctgcac atgtcttgta catgtgtagc ctgtgcatgt atgtcttgga 2040
cactgtacaa ggtacccctt tctggctctc ccatttcctg agaccacaga gagaggggag 2100
aagcctggga ttgacagaag cttctgccca cctacttttc tttcctcaga tcatccagaa 2160
gttcctcaag ggccaggact ttatctaata cctctgtgtg ctcctccttg gtgcctggcc 2220
tggcacacat caggagttca ataaatgtct gttgatgact gttgtacaca acaacaaaac 2280
aa 2282

<210> 5
<211> 932
<212> DNA
<213> Homo sapiens

<400> 5
gaggcagcag cagcaggagg aggcagagca cagcatcgtc gggaccagac tcgtctcagg 60
ccagttgcag ccttctcagc caaacgccga ccaaggaaaa ctcactacca tgagaattgc 120
agtgatttgc ttttgcctcc taggcatcac ctgtgccata ccagttaaac aggctgattc 180
tggaagttct gaggaaaagc agctttacaa caaataccca gatgctgtgg ccacatggct 240
aaaccctgac ccatctcaga agcagaatct cctagcccca cagaatgctg tgtcctctga 300
agaaaccaat gactttaaac aagagaccct tccaagtaag tccaacgaaa gccatgacca 360
catggatgat atggatgatg aagatgatga tgaccatgtg gacagccagg actccattga 420
ctcgaacgac tctgatgatg tagatgacac tgatgattct caccagtctg atgagtctca 480
ccattctgat gaatctgatg aactggtcac tgattttccc acggacctgc cagcaaccga 540
agttttcact ccagttgtcc ccacagtaga cacatatgat ggccgaggtg atagtgtggt 600
ttatggactg aggtcaaaat ctaagaagtt tcgcagacct gacatccagg taaatccttt 660
aacagacaca cctgatggtt ctgactagcg ctcaagtcta ggaaaccaca gtttgcatat 720
tcattcattc attcatccat tcattcatcc attcagcaag aattcattca tattctactt 780
tatgaccatt gaatacaaat ctttttctgc ttggcggttt ttgtaagtct acataatttc 840
tctctagatt tgattctcaa acacaattct acttttgaa atcctggatc agttattttc 900
agattaaaat aaatggaaaa caccaattat tt 932

<210> 6
<211> 1314
<212> DNA
<213> Homo sapiens

<400> 6
agcgtcggac taccgttggt ttccgcaact tcctggatta tcctcgccaa ggactttgca 60
atatattttt ccgccttttc tggaaggatt tcgctgcttc ccgaagtctt ggacgagcgc 120
tctagctctg tgggaaggtt ttgggctctc tggctcggat tttgcaattt ctccctgggg 180
actgccgtgg agccgcatcc actgtggatt ataattgcaa catgacgctg gaagagctcg 240
tggcgtgcga caacgcggcg cagaagatgc agacggtgac cgccgcggtg gaggagcttt 300
tggtggccgc tcagcgccag gatcgcctca cagtgggggt gtacgagtcg gccaagttga 360
tgaatgtgtg agtcagaccc ccttcccggg ctgggcgcgg gtgggacggg acctcccctc 420
cgctctggac gctttccgca cgcttgtctt gcatggagct gggacttccc caagtgcccc 480
ccgctgtgga tgcagagctt ctctgccgtt ttgtggatcg ggggctgccg tatcctgatg 540
tatcgtctgc aaacacccct cccgccgtgg gcctgtctcc ccctacccca tactttgaac 600
cgtgtgccct ccctcccccc caccgtcacc agcttgcaga ggcaatcccc tgcacccttg 660
cagtttcgaa ccctcacacg gacgcctgga agagccacgg cttggtggag gtggccagct 720
actgcgaaga aagccggggc aacaaccagt gggtccccta catctctctt caggaacgct 780
gaggcccttc ccagcagcag aatctgttga gttgctgcca caaacaaaaa atacaataaa 840
tatttgaacc ccctcccccc cagcacaacc cccccaaaac aacccaaccc acgaggacca 900
tcgggggcag agtcgttgga gactgaagag gaagaggagg aggagaaggg gagtgagcgg 960
ccgctgccgc cttccccatc acggagggtc cagactgtcc actcgggggt ggagtgagac 1020
tgactgcaag ccccaccctc cttgagactg gagctggcgt ctgcatacga gagacttggt 1080

tgaacttggt tggtccttgt ctgcaccctc gacaagacca cactttggga cttgggagct 1140
ggggctgaag ttgctctgta cccatgaact cccagtttgc gaattataga gacaatctat 1200
tttgttactt gcacttgtta ttcgaaccac tgagagcgag atgggaagca tagatatcta 1260
tatttttatt tctactatga gggccttgta ataaatttct aaagcctcaa aaaa 1314

<210> 7
<211> 2130
<212> DNA
<213> Homo sapiens

<400> 7
cgctgtgtct gcccggtctc tcctggggtc tccggttctg ccgcctcctg tccctccttc 60
cggctgcccc ggccagaggg gctcgaaggc gcgttggggc ccggggccac gctgggagac 120
acgccttcgg ccgcgcctaa ttcgagccag gcgcgggacg cgtcccccgg ccgggcggag 180
cgggagggga cgcccgccgc gctcggcctc cccgggcccc gacccctcct ttgtaatttg 240
aataaaacgc ctcccccgcc cgcgcgccgc cttaacccgc cgcctccgct ctccccggct 300
gcaggcggcg tgcaggacca gcggcggccg tgcaggcgga ggacttcggc gcggctcctc 360
ctgggtgtga ccccgggcgc gcccgccgcg cgacgatgag ggcgcggccg caggtctgcg 420
aggcgctgct cttcgccctg gcgctccaga ccggcgtgtg ctatggcatc aagtggctgg 480
cgctgtccaa gacaccatcg gccctggcac tgaaccagac gcaacactgc aagcagctgg 540
agggtctggt gtctgcacag gtgcagctgt gccgcagcaa cctggagctc atgcacacgg 600
tggtgcacgc cgcccgcgag gtcatgaagg cctgtcgccg ggcctttgcc gacatgcgct 660
ggaactgctc ctccattgag ctcgccccca actatttgct tgacctggag agagggaccc 720
gggagtcggc cttcgtgtat gcgctgtcgg ccgccgccat cagccacgcc atcgcccggg 780
cctgcacctc cggcgacctg cccggctgct cctgcggccc cgtcccaggt gagccacccg 840
ggcccgggaa ccgctgggga agatgtgcgg acaacctcag ctacgggctc ctcatggggg 900
ccaagttttc cgatgctcct atgaaggtga aaaaaacagg atcccaagcc aataaactga 960
tgcgtctaca caacagtgaa gtggggagac aggctctgcg cgcctctctg gaaatgaagt 1020
gtaagtgcca tggggtgtct ggctcctgct ccatccgcac ctgctggaag gggctgcagg 1080
agctgcagga tgtggctgct gacctcaaga cccgatacct gtcggccacc aaggtagtgc 1140
accgacccat gggcacccgc aagcacctgg tgcccaagga cctggatatc cggcctgtga 1200
aggactcgga actcgtctat ctgcagagct cacctgactt ctgcatgaag aatgagaagg 1260
tgggctccca cgggacacaa gacaggcagt gcaacaagac atccaacgga agcgacagct 1320
gcgaccttat gtgctgctac gtcacctgcc gcaggtgtga gcgtaccgtg gagcgctatg 1380
tctgcaagtg aggccctgcc ctccgcccca cgcaggagcg aggactctgc tcaaggaccc 1440
tcagcaactg gggccagggg cctggagaca ctccatggag ctctgcttgt gaattccaga 1500
tgccaggcat gggaggcggc ttgtgctttg ccttcacttg gaagccacca ggaacagaag 1560
gtctggccac cctggaagga gggcaggaca tcaaaggaaa ccgacaagat taaaaataac 1620
ttggcagcct gaggctctgg agtgcccaca ggctggtgta aggagcgggg cttgggatcg 1680
gtgagactga tacagacttg acctttcagg gccacagaga ccagcctccg ggaaggggtc 1740
tgcccgcctt cttcagaatg ttctgcggga ccccctggcc caccctgggg tctgagcctg 1800
ctgggcccac cacatggaat cactagcttg ggttgtaaat gttttctttt gtttttgct 1860
ttttcttcct ttgggatgtg gaagctacag aaatatttat aaaacatagc tttttctttg 1920
gggtggcact tctcaattcc tctttatata ttttatatat ataaatatat atgtatatat 1980
ataatgatct ctattttaaa actagctttt taagcagctg tatgaaataa atgctgagtg 2040
agccccagcc cgcccctgca gttcccggcc tcgtcaagtg aactcggcag accctggggc 2100
tggcagaggg agctctccag tttccgggca 2130

<210> 8
<211> 1847
<212> DNA
<213> Homo sapiens

<400> 8
cgctgtgtct gcccggtctc tcctggggtc tccggttctg ccgcctcctg tccctccttc 60
cggctgcccc ggccagaggg gctcgaaggc gcgttggggc ccggggccac gctgggagac 120
acgccttcgg ccgcgcctaa ttcgagccag gcgcgggacg cgtcccccgg ccgggcggag 180
cgggagggga cgcccgccgc gctcggcctc cccgggcccc gacccctcct ttgtaatttg 240
aataaaacgc ctcccccgcc cgcgcgccgc cttaacccgc cgcctccgct ctccccggct 300

gcaggcggcg tgcaggacca gcggcggccg tgcaggcgga ggacttcggc gcggctcctc 360
ctgggtgtga ccccgggcgc gcccgccgcg cgacgatgag ggcgcggccg caggtctgcg 420
aggcgctgct cttcgccctg gcgctccaga ccggcgtgtg ctatggcatc aagtggctgg 480
cgctgtccaa gacaccatcg gccctggcac tgaaccagac gcaacactgc aagcagctgg 540
agggtctggt gtctgcacag gtgcagctgt gccgcagcaa cctggagctc atgcacacgg 600
tggtgcacgc cgcccgcgag gtcatgaagg cctgtcgccg ggcctttgcc gacatgcgct 660
ggaactgctc ctccattgag ctcgccccca actatttgct tgacctggag agagggaccc 720
gggagtcggc cttcgtgtat gcgctgctga cctcaagacc cgatacctgt cggccaccaa 780
ggtagtgcac cgacccatgg gcacccgcaa gcacctggtg cccaaggacc tggatatccg 840
gcctgtgaag gactcggaac tcgtctatct gcagagctca cctgacttct gcatgaagaa 900
tgagaaggtg ggctcccacg ggacacaaga caggcagtgc aacaagacat ccaacggaag 960
cgacagctgc gaccttatgt gctgcgggcg tggctacaac ccctacacag accgcgtggt 1020
cgagcggtgc cactgtaagt accactggtg ctgctacgtc acctgccgca ggtgtgagcg 1080
taccgtggag cgctatgtct gcaagtgagg ccctgccctc cgccccacgc aggagcgagg 1140
actctgctca aggaccctca gcaactgggg ccaggggcct ggagacactc catggagctc 1200
tgcttgtgaa ttccagatgc caggcatggg aggcggcttg tgctttgcct tcacttggaa 1260
gccaccagga acagaaggtc tggccaccct ggaaggaggg caggacatca aaggaaaccg 1320
acaagattaa aaataacttg gcagcctgag gctctggagt gcccacaggc tggtgtaagg 1380
agcggggctt gggatcggtg agactgatac agacttgacc tttcagggcc acagagacca 1440
gcctccggga aggggtctgc ccgccttctt cagaatgttc tgcgggaccc cctggcccac 1500
cctggggtct gagcctgctg ggcccaccac atggaatcac tagcttgggt tgtaaatgtt 1560
ttcttttgtt ttttgctttt tcttcctttg ggatgtggaa gctacagaaa tatttataaa 1620
acatagcttt ttctttgggg tggcacttct caattcctct ttatatattt tatatatata 1680
aatatatatg tatatatata atgatctcta ttttaaaact agctttttaa gcagctgtat 1740
gaaataaatg ctgagtgagc cccagcccgc ccctgcagtt cccggcctcg tcaagtgaac 1800
tcggcagacc ctggggctgg cagagggagc tctccagttt ccgggca 1847

<210> 9
<211> 2369
<212> DNA
<213> Homo sapiens

<400> 9
gaattccgcc agccccgcca gtccccgcgc agtccccgcg cagtcccagc gccaccgggc 60
agcagcggcg ccgtgctcgc tccagggcgc aaccatgtcg ccatttcttc ggattggctt 120
gtccaacttt gactgcgggt cctgccagtc ttgtcagggc gaggctgtta acccttactg 180
tgctgtgctc gtcaaagagt atgtcgaatc agagaacggg cagatgtata tccagaaaaa 240
gcctaccatg tacccaccct gggacagcac ttttgatgcc catatcaaca agggaagagt 300
catgcagatc attgtgaaag gcaaaaacgt ggacctcatc tctgaaacca ccgtggagct 360
ctactcgctg gctgagaggt gcaggaagaa caacgggaag acagaaatat ggttagagct 420
gaaacctcaa ggccgaatgc taatgaatgc aagatacttt ctggaaatga gtgacacaaa 480
ggacatgaat gaatttgaga cggaaggctt ctttgctttg catcagcgcc ggggtgccat 540
caagcaggca aaggtccacc acgtcaagtg ccacgagttc actgccacct tcttcccaca 600
gcccacattt tgctctgtct gccacgagtt tgtctggggc ctgaacaaac agggctacca 660
gtgccgacaa tgcaatgcag caattcacaa gaagtgtatt gataaagtta tagcaaagtg 720
cacaggatca gctatcaata gccgagaaac catgttccac aaggagagat tcaaaattga 780
catgccacac agatttaaag tctacaatta caagagcccg accttctgtg aacactgtgg 840
gaccctgctg tggggactgg cacggcaagg actcaagtgt gatgcatgtg gcatgaatgt 900
gcatcataga tgccagacaa aggtggccaa cctttgtggc ataaaccaga agctaatggc 960
tgaagcgctg gccatgattg agagcactca acaggctcgc tgcttaagag atactgaaca 1020
gatcttcaga gaaggtccgg ttgaaattgg tctcccatgc tccatcaaaa atgaagcaag 1080
gccgccatgt ttaccgacac cgggaaaaag agagcctcag ggcatttcct gggagtctcc 1140
gttggatgag gtggataaaa tgtgccatct tccagaacct gaactgaaca aagaaagacc 1200
atctctgcag attaaactaa aaattgagga ttttatcttg cacaaaatgt tggggaaagg 1260
aagttttggc aaggtcttcc tggcagaatt caagaaaacc aatcaatttt tcgcaataaa 1320
ggccttaaag aaagatgtgg tcttgatgga cgatgatgtt gagtgcacga tggtagagaa 1380
gagagttctt tccttggcct gggagcatcc gtttctgacg cacatgtttt gtacattcca 1440
gaccaaggaa aacctctttt ttgtgatgga gtacctcaac ggaggggact taatgtacca 1500
catccaaagc tgccacaagt tcgacctttc cagagcgacg ttttatgctg ctgaaatcat 1560
tcttggtctg cagttccttc attccaaagg aatagtctac agggacctga agctagataa 1620

catcctgtta gacaaagatg gacatatcaa gatcgcggat tttggaatgt gcaaggagaa 1680
catgttagga gatgccaaga cgaatacctt ctgtgggaca cctgactaca tcgccccaga 1740
gatcttgctg ggtcagaaat acaaccactc tgtggactgg tggtccttcg gggttctcct 1800
ttatgaaatg ctgattggtc agtcgccttt ccacgggcag gatgaggagg agctcttcca 1860
ctccatccgc atggacaatc ccttttaccc acggtggctg gagaaggaag caaaggacct 1920
tctggtgaag gtaagaagct gaaggtaaga agcgaagcca agagcgtctt cataagacga 1980
gcattaggtc ttctggtcag ttttctgttc ctcttagttt ccaacttgca tgtggcaaac 2040
aatgattatt attgaactgg gtttaaatgg gatgtgcacc gtctgtgttt taatagaggc 2100
accaatatta tgagcattaa atgtcaaaat gagtgtaaga gaaaccctca tgtgcatcag 2160
ttataacata acggccccag gaaccagttc catggacctt gaatacgctc acctggagat 2220
gtagttggtt cattaaacaa gcacagtgtg tggcttaaaa atcaatcttc tagctacttg 2280
ggaggttgag gcaggaggat tgaagttgga agtgtgaggt cagcctgggc aatgtatcga 2340
gacccctgtc tccaaaacaa taaagggga 2369

<210> 10
<211> 1101
<212> DNA
<213> Homo sapiens

<400> 10
ctccttagtc gaggcaagac gtgcgcccga gccccgccga accgaggcca cccggagccg 60
tgcccagtcc acgccggccg tgcccggcgg ccttaagaac caggcaacct ctgccttctt 120
ccctcttcca ctcggagtcg cgctccgcgc gccctcactg cagcccctgc gtcgccggga 180
ccctcgcgcg cgaccagccg aatcgctcct gcagcagagc caacatgccc atcactcgga 240
tgcgcatgag accctggcta gagatgcaga ttaattccaa ccaaatcccg gggctcatct 300
ggattaataa agaggagatg atcttccaga tcccatggaa gcatgctgcc aagcatggct 360
gggacatcaa caaggatgcc tgtttgttcc ggagctgggc cattcacaca ggccgataca 420
aagcagggga aaaggagcca gatcccaaga cgtggaaggc caactttcgc tgtgccatga 480
actccctgcc agatatcgag gaggtgaaag accagagcag gaacaagggc agctcagctg 540
tgcgagtgta ccggatgctt ccacctctca ccaagaacca gagaaaagaa agaaagtcga 600
agtccagccg agatgctaag agcaaggcca agaggaagtc atgtggggat tccagccctg 660
ataccttctc tgatggactc agcagctcca ctctgcctga tgaccacagc agctacacag 720
ttccaggcta catgcaggac ttggaggtgg agcaggccct gactccagca ctgtcgccat 780
gtgctgtcag cagcactctc cccgactggc acatcccagt ggaagttgtg ccggacagca 840
ccagtgatct gtacaacttc caggtgtcac ccatgccctc cacctctgaa gctacaacag 900
atgaggatga ggaagggaaa ttacctgagg acatcatgaa gctcttggag cagtcggagt 960
ggcagccaac aaacgtggat gggaaggggt acctactcaa tgaacctgga gtccagccca 1020
cctctgtcta tggagacttt agctgtaagg aggagccaga aattgacagc ccaggggtga 1080
agaaggcccc tggatcctta t 1101

<210> 11
<211> 4628
<212> DNA
<213> Homo sapiens

<400> 11
cctcttgcgg ccacaggcgc ggcgtcctcg gcggcgggcg gcagctagcg ggagccggga 60
cgccggtgca gccgcagcgc gcggaggaac ccgggtgtgc cgggagctgg gcggccacgt 120
ccggwcggga ccgagacccc tcgtagcgca ttgcggcgac ctcgccttcc ccggccgcga 180
gcgcgccgct gcttgaaaag ccgcggaacc caaggacttt tctccggtcc gagctcgggg 240
cgccccgcag gcgcacggta cccgtgctgc agtcgggcac gccgcgggcg ccgggggcct 300
ccgcagggcg atggagcccg gtctgcaagg aaagtgaggc gccgccgctg cgttctggag 360
gaggggggca caaggtctgg agaccccggg tggcggacgg gagccctccc cccgccccgc 420
ctccggggca ccagctccgg ctccattgtt cccgcccggg ctggaggcgc cgagcaccga 480
gcgccgccgg gagtcgagcg ccggccgcgg agctcttgcg accccgccag gacccgaaca 540
gagcccgggg gcggcgggcc ggagccgggg acgcgggcac acgcccgctc gcacaagcca 600
cggcggactc tcccgaggcg gaacctccac gccgagcgag ggtcagtttg aaaaggagga 660
tcgagctcac tgtggagtat ccatggagat gtggagcctt gtcaccaacc tctaactgca 720
gaactgggat gtggagctgg aagtgcctcc tcttctgggc tgtgctggtc acagccacac 780

tctgcaccgc taggccgtcc ccgaccttgc ctgaacaagc ccagccctgg ggagcccctg 840
tggaagtgga gtccttcctg gtccaccccg gtgacctgct gcagcttcgc tgtcggctgc 900
gggacgatgt gcagagcatc aactggctgc gggacggggt gcagctggcg gaaagcaacc 960
gcacccgcat cacaggggag gaggtggagg tgcaggactc cgtgcccgca gactccggcc 1020
tctatgcttg cgtaaccagc agcccctcgg gcagtgacac cacctacttc tccgtcaatg 1080
tttcagatgc tctcccctcc tcggaggatg atgatgatga tgatgactcc tcttcagagg 1140
agaaagaaac agataacacc aaaccaaacc gtatgcccgt agctccatat tggacatccc 1200
cagaaaagat ggaaaagaaa ttgcatgcag tgccggctgc caagacagtg aagttcaaat 1260
gcccttccag tgggacccca aaccccacac tgcgctggtt gaaaaatggc aaagaattca 1320
aacctgacca cagaattgga ggctacaagg tccgttatgc cacctggagc atcataatgg 1380
actctgtggt gccctctgac aagggcaact acacctgcat tgtggagaat gagtacggca 1440
gcatcaacca cacataccag ctggatgtcg tggagcggtc ccctcaccgg cccatcctgc 1500
aagcagggtt gcccgccaac aaaacagtgg ccctgggtag caacgtggag ttcatgtgta 1560
aggtgtacag tgacccgcag ccgcacatcc agtggctaaa gcacatcgag gtgaatggga 1620
gcaagattgg cccagacaac ctgccttatg tccagatctt gaagactgct ggagttaata 1680
ccaccgacaa agagatggag gtgcttcact taagaaatgt ctcctttgag gacgcagggg 1740
agtatacgtg cttggcgggt aactctatcg gactctccca tcactctgca tggttgaccg 1800
ttctggaagc cctggaagag aggccggcag tgatgacctc gcccctgtac ctggagatca 1860
tcatctattg cacaggggcc ttcctcatct cctgcatggt ggggtcggtc atcgtctaca 1920
agatgaagag tggtaccaag aagagtgact tccacagcca gatggctgtg cacaagctgg 1980
ccaagagcat ccctctgcgc agacaggtaa cagtgtctgc tgactccagt gcatccatga 2040
actctggggt tcttctggtt cggccatcac ggctctcctc cagtgggact cccatgctag 2100
caggggtctc tgagtatgag cttcccgaag accctcgctg ggagctgcct cgggacagac 2160
tggtcttagg caaacccctg ggagagggct gctttgggca ggtggtgttg gcagaggcta 2220
tcgggctgga caaggacaaa cccaaccgtg tgaccaaagt ggctgtgaag atgttgaagt 2280
cggacgcaac agagaaagac ttgtcagacc tgatctcaga aatggagatg atgaagatga 2340
tcgggaagca taagaatatc atcaacctgc tgggggcctg cacgcaggat ggtcccttgt 2400
atgtcatcgt ggagtatgcc tccaagggca acctgcggga gtacctgcag gcccggaggc 2460
ccccagggct ggaatactgc tacaacccca gccacaaccc agaggagcag ctctcctcca 2520
aggacctggt gtcctgcgcc taccaggtgg cccgaggcat ggagtatctg gcctccaaga 2580
agtgcataca ccgagacctg gcagccagga atgtcctggt gacagaggac aatgtgatga 2640
agatagcaga ctttggcctc gcacgggaca ttcaccacat cgactactat aaaaagacaa 2700
ccaacggccg actgcctgtg aagtggatgg cacccgaggc attatttgac cggatctaca 2760
cccaccagag tgatgtgtgg tctttcgggg tgccccatac cccggtgtgc ctgtggagga 2820
acttttcaag ctgctgaagg agggtcaccg catggacaag cccagtaact gcaccaacga 2880
gctgtacatg atgatgcggg actgctggca tgcagtgccc tcacagagac ccaccttcaa 2940
gcagctggtg gaagacctgg accgcatcgt ggccttgacc tccaaccagg agtacctgga 3000
cctgtccatg cccctggacc agtactcccc cagctttccc gacacccgga gctctacgtg 3060
ctcctcaggg gaggattccg tcttctctca tgagccgctg cccgaggagc cctgcctgcc 3120
ccgacaccca gcccagcttg ccaatggcgg actcaaacgc cgctgactgc cacccacacg 3180
ccctccccag actccaccgt cagctgtaac cctcacccac agcccctgct gggcccacca 3240
cctgtccgtc cctgtccccc ttcctgctgg caggagccgg ctgcctacca ggggccttcc 3300
tgtgtggcct gccttcaccc cactcagctc acctctccct ccacctcctc tccacctgct 3360
ggtgagaggt gcaaagaggc agatctttgc tgccagccac ttcatccccc cccagatgtt 3420
ggaccaacac ccctccctgc caccaggcac tgcctggagg gcagggagtg ggagccaatg 3480
aacaggcatg caagtgagag cttcctgagc tttctcctgt cggtttggtc tgttttgcct 3540
tcacccataa gcccctcgca ctctggtggc aggtgccttg tcctcagggc tacagcagta 3600
gggaggtcag tgcttcgtgc ctcgattgaa ggtgacctct gccccagata ggtggtgcca 3660
gtggcttatt aattccgata ctagtttgct ttgctgacca aatgcctggt accagaggat 3720
ggtgaggcga aggccaggtt gggggcagtg ttgtggccct ggggcccagc cccaaactgg 3780
gggctctgta tatagctatg aagaaaacac aaagtgtata aatctgagta tatatttaca 3840
tgtcttttta aaagggtcgt taccagagat ttacccatcg ggtaagatgc tcctggtggc 3900
tgggaggcat cagttgctat atattaaaaa caaaaaagaa aaaaaaggaa aatgttttta 3960
aaaaggtcat atatttttg ctacttttgc tgttttattt ttttaaatta tgttctaaac 4020
ctattttcag tttaggtccc tcaataaaaa ttgctgctgc ttcatttatc tatgggctgt 4080
atgaaaaggg tgggaatgtc cactggaaag aagggacacc cacgggccct ggggctaggt 4140
ctgtcccgag ggcaccgcat gctcccggcg caggttcctt gtaacctctt cttcctaggt 4200
cctgcaccca gacctcacga cgcacctcct gcctctccgc tgcttttgga aagtcagaaa 4260
aagaagatgt ctgcttcgag ggcaggaacc ccatccatgc agtagaggcg ctgggcagag 4320
agtcaaggcc cagcagccat cgaccatgga tggtttcctc caagggaaac cggtggggtt 4380
tgggctgggg agggggcacc tacctaggga ttagccacgg ggtagagcta cagtgattaa 4440

gaggaaagca agggcgtgag ccaccacgcc tggcattaat ttgtcctttt ttaagatatg 4500
gggtctcact atgttgccca ggctggtctt gaactcctgg gctcaagtga tcctcctgcc 4560
ttagcctccc aaagtgctgg gattacaggc gtgagccact gtgcccagcc tgatgtgttc 4620
ttaattta 4628

<210> 12
<211> 1418
<212> DNA
<213> Homo sapiens

<400> 12
ccacgtgggg gctcagcgtg cacccttctt tgtgctcggg ttaggaggag ctaggctgcc 60
atcgggccgg tgcagatacg gggttgctct tttgctcata agaggggctt cgctggcagt 120
ctgaacggca agcttgagtc aggacccttа attaagatcc tcaattggct ggagggcaga 180
tctcgcgagt agggcaacgc ggtaaaaata ttgcttcggt gggtgacgcg gtacagctgc 240
ccaagggcgt tcgtaacggg aatgccgaag cgtgggaaaa agggagcggt ggcggaagac 300
ggggatgagc tcaggacaga gccagaggcc aagaagagta agacggccgc aaagaaaaat 360
gacaaagagg cagcaggaga gggcccagcc ctgtatgagg acccccaga tcagaaaacc 420
tcacccagtg gcaaacctgc cacactcaag atctgctctt ggaatgtgga tgggcttcga 480
gcctggatta agaagaaagg attagattgg gtaaaggaag aagccccaga tatactgtgc 540
cttcaagaga ccaaatgttc agagaacaaa ctaccagctg aacttcagga gctgcctgga 600
ctctctcatc aatactggtc agctccttcg gacaaggaag ggtacagtgg cgtgggcctg 660
ctttcccgcc agtgcccact caaagtttct tacggcatag catatgtacc taatgcaggc 720
cgaggtctgg tacgactgga gtaccggcag cgctgggatg aagcctttcg caagttcctg 780
aagggcctgg cttcccgaaa gccccttgtg ctgtgtggag acctcaatgt ggcacatgaa 840
gaaattgacc ttcgcaaccc caaggggaac aaaaagaatg ctggcttcac gccacaagag 900
cgccaaggct tcggggaatt actgcaggct gtgccactgg ctgacagctt taggcacctc 960
taccccaaca caccctatgc ctacaccttt tggacttata tgatgaatgc tcgatccaag 1020
aatgttggtt ggcgccttga ttacttttg ttgtcccact ctctgttacc tgcattgtgt 1080
gacagcaaga tccgttccaa ggccctcggc agtgatcact gtcctatcac cctataccta 1140
gcactgtgac accacccta aatcactttg agcctgggaa ataagccccc tcaactacca 1200
ttccttcttt aaacactctt cagagaaatc tgcattctat ttctcatgta taaaactagg 1260
aatcctccaa ccaggctcct gtgatagagt tcttttaagc ccaagatttt ttatttgagg 1320
gttttttgtt ttttaaaaaa aaattgaaca aagactacta atgactttgt ttgaattatc 1380
cacatgaaaa taaagagcca tagtttcagc gtcgtacc 1418

<210> 13
<211> 1558
<212> DNA
<213> Homo sapiens

<400> 13
ccacgtgggg gctcagcgtg cacccttctt tgtgctcggg ttaggaggag ctaggctgcc 60
atcgggccgg tgcagatacg gggttgctct tttgctcata agaggggctt cgctggcagt 120
ctgaacggca agcttgagtc aggacccttа attaagatcc tcaattggct ggagggcaga 180
tctcgcgagt agggcaacgc ggtaaaaata ttgcttcggt gggtgacgcg gtacagctgc 240
ccaagggcgt tcgtaacggg aatgccgaag cgtgggaaaa agggagcggt ggcggaagac 300
ggggatgagc tcaggacagg taagggaatg aaatcagccc ttcttcctag aactgcggcg 360
ggggtgtttg tcattccctt gatgtacgag agccagaggc caagaagagt aagacggccg 420
caaagaaaaa tgacaaagag gcagcaggag agggcccagc cctgtatgag gacccccag 480
atcagaaaac ctcacccagt ggcaaacctg ccacactcaa gatctgctct tggaatgtgg 540
atgggcttcg agcctggatt aagaagaaag gattagattg ggtaaaggaa gaagccccag 600
atatactgtg ccttcaagag accaaatgtt cagagaacaa actaccagct gaacttcagg 660
agctgcctgg actctctcat caatactggt cagctccttc ggacaaggaa gggtacagtg 720
gcgtgggcct gctttcccgc cagtgcccac tcaaagtttc ttacggcata ggcgatgagg 780
agcatgatca ggaaggccgg gtgattgtgg ctgaatttga ctcgtttgtg ctggtaacag 840
catatgtacc taatgcaggc cgaggtctgg tacgactgga gtaccggcag cgctgggatg 900
aagcctttcg caagttcctg aagggcctgg cttcccgaaa gccccttgtg ctgtgtggag 960
acctcaatgt ggcacatgaa gaaattgacc ttcgcaaccc caaggggaac aaaaagaatg 1020

ctggcttcac gccacaagag cgccaaggct tcggggaatt actgcaggct gtgccactgg 1080
ctgacagctt taggcacctc taccccaaca caccctatgc ctacaccttt tggacttata 1140
tgatgaatgc tcgatccaag aatgttggtt ggcgccttga ttacttttg ttgtcccact 1200
ctctgttacc tgcattgtgt gacagcaaga tccgttccaa ggccctcggc agtgatcact 1260
gtcctatcac cctataccta gcactgtgac accacccta aatcactttg agcctgggaa 1320
ataagccccc tcaactacca ttccttcttt aaacactctt cagagaaatc tgcattctat 1380
ttctcatgta taaaactagg aatcctccaa ccaggctcct gtgatagagt tcttttaagc 1440
ccaagatttt ttatttgagg gttttttgtt ttttaaaaaa aaattgaaca aagactacta 1500
atgactttgt ttgaattatc cacatgaaaa taaagagcca tagtttcagc gtcgtacc 1558

<210> 14
<211> 1911
<212> DNA
<213> Homo sapiens

<400> 14
tgccgccgtc ccgcccgcca gcgccccagc gaggaagcag cgcgcagccc gcggcccagc 60
gcacccgcag cagcgcccgc agctcgtccg cgccatgttc caggcggccg agcgccccca 120
ggagtgggcc atggagggcc cccgcgacgg gctgaagaag gagcggctac tggacgaccg 180
ccacgacagc ggcctggact ccatgaaaga cgaggagtac gagcagatgg tcaaggagct 240
gcaggagatc cgcctcgagc cgcaggaggt gccgcgcggc tcggagccct ggaagcagca 300
gctcaccgag gacggggact cgttcctgca cttggccatc atccatgaag aaaaggcact 360
gaccatggaa gtgatccgcc aggtgaaggg agacctggcc ttcctcaact tccagaacaa 420
cctgcagcag actccactcc acttggctgt gatcaccaac cagccagaaa ttgctgaggc 480
acttctggga gctggctgtg atcctgagct ccgagacttt cgaggaaata ccccctaca 540
ccttgcctgt gagcagggct gcctggccag cgtgggagtc ctgactcagt cctgcaccac 600
cccgcacctc cactccatcc tgaaggctac caactacaat ggccacacgt gtctacactt 660
agcctctatc catggctacc tgggcatcgt ggagcttttg gtgtccttgg gtgctgatgt 720
caatgctcag gagccctgta atggccggac tgcccttcac ctcgcagtgg acctgcaaaa 780
tcctgacctg gtgtcactcc tgttgaagtg tggggctgat gtcaacagag ttacctacca 840
gggctattct ccctaccagc tcacctgggg ccgcccaagc acccggatac agcagcagct 900
gggccagctg acactagaaa accttcagat gctgccagag agtgaggatg aggagagcta 960
tgacacagag tcagagttca cggagttcac agaggacgag gtgagtctgt gaactcttcg 1020
gcgctctaac taatgaggtg ccattccctt caccctccca ggcccctaga gctgctcctt 1080
atcagagggg tatctacata atgagtctct caaatttctg tgcataacca gtatcccaag 1140
aatgtacctg ccccccccct ttttttaata gcttactctt tttttaaaga gaagcattaa 1200
aggcaaactc cctcagcctg taaagttcat tatatttggg ctatggagaa tggagtccaa 1260
gagttatttc cagtagtggc ctccccatcc cggtagcttg gcagagctcc gctccggaag 1320
cttaacgtgt ctttttccc cttgttttca gctgccctat gatgactgtg tgtttggagg 1380
ccagcgtctg acgttatgag cgcaaagggg ctgaaagaac atggacttgt atatttgtac 1440
aaaaaaaaag ttttatttt ctaaaaaaag aaaaaagaag aaaaaattta aagggtgtac 1500
ttatatccac actgcacact gcctggccca aaacgtctta ttgtggtagg atcagccctc 1560
attttgttgc ttttgtgaac tttttgtagg ggacgagaaa gatcattgaa attctgagaa 1620
aacttctttt aaacctcacc tttgtggggt ttttggagaa ggttatcaaa aatttcatgg 1680
aaggaccaca ttttatattt attgtgcttc gagtgactga ccccagtggt atcctgtgac 1740
atgtaacagc caggagtgtt aagcgttcag tgatgtgggg tgaaaagtta ctacctgtca 1800
aggtttgtgt taccctcctg taaatggtgt acataatgta ttgttggtaa ttattttggt 1860
acttttatga tgtatattta ttaaacagat ttttacaaat ggaanaaaga n 1911

<210> 15
<211> 1476
<212> DNA
<213> Homo sapiens

<400> 15
tgccgccgtc ccgcccgcca gcgccccagc gaggaagcag cgcgcagccc gcggcccagc 60
gcacccgcag cagcgcccgc agctcgtccg cgccatgttc caggcggccg agcgccccca 120
ggagtgggcc atggagggcc cccgcgacgg gctgaagaag gagcggctac tggacgaccg 180
ccacgacagc ggcctggact ccatgaaaga cgaggagtac gagcagatgg tcaaggagct 240

gcaggagatc cgcctcgagc cgcaggaggt gccgcgcggc tcggagccct ggaagcagca 300
gctcaccgag gacggggact cgttcctgca cttggccatc atccatgaag aaaaggcact 360
gaccatggaa gtgatccgcc aggtgaaggg agacctggcc ttcctcaact tccagaacaa 420
cctgcagcag actccactcc acttggctgt gatcaccaac cagccagaaa ttgctgaggc 480
acttctggga gctggctgtg atcctgagct ccgagacttt cgaggaaata ccccccctaca 540
ccttgcctgt gagcagggct gcctggccag cgtgggagtc ctgactcagt cctgcaccac 600
cccgcacctc cactccatcc tgaaggctac caactacaat ggtcaggagc cctgtaatgg 660
ccggactgcc cttcacctcg cagtggacct gcaaaatcct gacctggtgt cactcctgtt 720
gaagtgtggg gctgatgtca acagagttac ctaccagggc tattctccct accagctcac 780
ctggggccgc ccaagcaccc ggatacagca gcagctgggc cagctgacac tagaaaacct 840
tcagatgctg ccagagagtg aggatgagga gagctatgac acagagtcag agttcacgga 900
gttcacagag gacgagctgc cctatgatga ctgtgtgttt ggaggccagc gtctgacgtt 960
atgagcgcaa aggggctgaa agaacatgga cttgtatatt tgtacaaaaa aaaagtttta 1020
tttttctaaa aaaagaaaaa agaagaaaaa atttaaaggg tgtacttata tccacactgc 1080
acactgcctg gcccaaaacg tcttattgtg gtaggatcag ccctcatttt gttgcttttg 1140
tgaacttttt gtaggggacg agaaagatca ttgaaattct gagaaaactt cttttaaacc 1200
tcacctttgt ggggtttttg gagaaggtta tcaaaaattt catggaagga ccacatttta 1260
tatttattgt gcttcgagtg actgacccca gtggtatcct gtgacatgta acagccagga 1320
gtgttaagcg ttcagtgatg tggggtgaaa agttactacc tgtcaaggtt tgtgttaccc 1380
tcctgtaaat ggtgtacata atgtattgtt ggtaattatt ttggtacttt tatgatgtat 1440
atttattaaa cagattttta caaatggaan aaagan 1476

<210> 16
<211> 2913
<212> DNA
<213> Homo sapiens

<400> 16
aagcggcagg agcagcgttg gcaccggcga accatggctg ggattttcta tttcgcccta 60
ttttcgtgtc tcttcgggat ttgcgacgct gtcacaggtt ccagggtata ccccgcgaat 120
gaagttacct tattggattc cagatctgtt cagggagaac ttgggtggat agcaagccct 180
ctggaaggag ggtgggagga agtgagtatc atggatgaaa aaaatacacc aatccgaacc 240
taccaagtgt gcaatgtgat ggaacccagc cagaataact ggctacgaac tgattggatc 300
acccgagaag gggctcagag ggtgtatatt gagattaaat tcaccttgag ggactgcaat 360
agtcttccgg gcgtcatggg gacttgcaag gagacgttta acctgtacta ctatgaatca 420
gacaacgaca aagagcgttt catcagagag aaccagtttg tcaaaattga caccattgct 480
gctgatgaga gcttcaccca agtggacatt ggtgacagaa tcatgaagct gaacaccgag 540
atccgggatg tagggccatt aagcaaaaag gggttttacc tggcttttca ggatgtgggg 600
gcctgcatcg ccctggtatc agtccgtgtg ttctataaaa agtgtccact cacagtccgc 660
aatctggccc agtttcctga caccatcaca ggggctgata cgtcttccct ggtggaagtt 720
cgaggctcct gtgtcaacaa ctcagaagag aaagatgtgc caaaaatgta ctgtggggca 780
gatggtgaat ggctggtacc cattggcaac tgcctatgca acgctgggca tgaggagcgg 840
agcggagaat gccaagcttg caaaattgga tattacaagg ctctctccac ggatgccacc 900
tgtgccaagt gcccacccca cagctactct gtctgggaag gagccacctc gtgcacctgt 960
gaccgaggct ttttcagagc tgacaacgat gctgcctcta tgccctgcac ccgtccacca 1020
tctgctcccc tgaacttgat ttcaaatgtc aacgagacat ctgtgaactt ggaatggagt 1080
agccctcaga atacaggtgg ccgccaggac atttcctata atgtggtatg caagaaatgt 1140
ggagctggtg accccagcaa gtgccgaccc tgtggaagtg gggtccacta caccccacag 1200
cagaatggct tgaagaccac caaagtctcc atcactgacc tcctagctca taccaattac 1260
acctttgaaa tctgggctgt gaatggagtg tccaaatata accctaaccc agaccaatca 1320
gtttctgtca ctgtgaccac caaccaagca gcaccatcat ccattgcttt ggtccaggct 1380
aaagaagtca caagatacag tgtggcactg gcttggctgg aaccagatcg gcccaatggg 1440
gtaatcctgg aatatgaagt caagtattat gagaaggatc agaatgagcg aagctatcgt 1500
atagttcgga cagctgccag gaacacagat atcaaaggcc tgaaccctct cacttcctat 1560
gttttccacg tgcgagccag gacagcagct ggctatggag acttcagtga gcccttggag 1620
gttacaacca acacagtgcc ttcccggatc attggagatg gggctaactc cacagtcctt 1680
ctggtctctg tctcgggcag tgtggtgctg gtggtaattc tcattgcagc ttttgtcatc 1740
agccggagac ggagtaaata cagtaaagcc aaacaagaag cggatgaaga gaaacatttg 1800
aatcaaggtg taagaacata tgtggacccc tttacgtacg aagatcccaa ccaagcagtg 1860
cgagagtttg ccaaagaaat tgacgcatcc tgcattaaga ttgaaaaagt tataggagtt 1920

ggtgaatttg gtgaggtatg cagtgggcgt ctcaaagtgc ctggcaagag agagatctgt 1980
gtggctatca agactctgaa agctggttat acagacaaac agaggagaga cttcctgagt 2040
gaggccagca tcatgggaca gtttgaccat ccgaacatca ttcacttgga aggcgtggtc 2100
actaaatgta aaccagtaat gatcataaca gagtacatgg agaatggctc cttggatgca 2160
ttcctcagga aaaatgatgg cagatttaca gtcattcagc tggtgggcat gcttcgtggc 2220
attgggtctg ggatgaagta tttatctgat atgagctatg tgcatcgtga tctggccgca 2280
cggaacatcc tggtgaacag caacttggtc tgcaaagtgt ctgattttgg catgtcccga 2340
gtgcttgagg atgatccgga agcagcttac accaccaggg gtggcaagat tcctatccgg 2400
tggactgcgc cagaagcaat tgcctatcgt aaattcacat cagcaagtga tgtatggagc 2460
tatggaatcg ttatgtggga agtgatgtcg tacggggaga ggccctattg ggatatgtcc 2520
aatcaagata cctaacactg ccttgttgga tccaagctcc cctgaattct ctgctgtggt 2580
atcagtgggc gattggctcc aggccattaa aatggaccgg tataaggata acttcacagc 2640
tgctggttat accacactag aggctgtggt gcacgtgaac caggaggacc tggcaagaat 2700
tggtatcaca gccatcacgc accagaataa gattttgagc agtgtccagg caatgcgaac 2760
ccaaatgcag cagatgcacg gcagaatggt tcccgtctga gccagtactg aataaactca 2820
aaactcttga aattagttta cctcatccat gcactttaat tgaagaactg cactttttt 2880
acttcgtctt cgccctctga aattaaagaa atg 2913

<210> 17
<211> 3695
<212> DNA
<213> Homo sapiens

<400> 17
ccgtttcctc ccctcccctc cactcggccg tccctccttc ctcctccctc ctccctcctc 60
ctcccgctcc tgaagagcgc gccgcgtggg ggacggcccg gttacttcct ccagagactg 120
acgagtgcgg tgtcgctcca gctcagagct cccggagccg cccggccagc gtccggcctc 180
cctgatcgtc tctggccggc gccctcgccc tcgcccggcg cgcaccgagc agccgcgggc 240
gccgagcagc caccgtcccg accaagcgcc ggccctgccc gcagcggcag gatgaatgat 300
ttcggaatca agaatatgga ccaggtagcc cctgtggcta acagttacag agggacactc 360
aagcgccagc cagcctttga caccttgat gggtccctgt ttgctgtttt tccttctcta 420
aatgaagagc aaacactgca agaagtgcca acaggcttgg attccatttc tcatgactcc 480
gccaactgtg aattgccttt gttaaccccg tgcagcaagg ctgtgatgag tcaagcctta 540
aaagctacct tcagtggctt ctctgggcca ccaatgagtt cagtctggtg aacgtgaatc 600
tgcagaggtt cggcatgaat ggccagatgc tgtgtaacct tggcaaggaa cgctttctgg 660
agctggcacc tgactttgtg ggtgacattc tctgggaaca tctggagcaa atgatcaaag 720
aaaaccaaga aaagacagaa gatcaatatg aagaaaattc acacctcacc tccgttcctc 780
attggattaa cagcaataca ttaggttttg gcacagagca ggcgccctat ggaatgcaga 840
cacagaatta ccccaaaggc ggcctcctgg acagcatgtg tccggcctcc acacccagcg 900
tactcagctc tgagcaggag tttcagatgt tccccaagtc tcggctcagc tccgtcagcg 960
tcacctactg ctctgtcagt caggacttcc caggcagcaa cttgaatttg ctcaccaaca 1020
attctgggac gcccaaagac cacgactccc ctgagaacgg tgcggacagc ttcgagagct 1080
cagactccct cctccagtcc tggaacagcc agtcgtcctt gctggatgtg caacgggttc 1140
cttccttcga gagcttcgaa gatgactgca gccagtctct ctgcctcaat aagccaacca 1200
tgtctttcaa ggattacatc caagagagga gtgacccggt ggagcaaggc aaaccagtta 1260
tacctgcagc tgtgctggcc ggcttcacag gaagtggacc tattcagctg tggcagtttc 1320
tcctggagct gctatcagac aaatcctgcc agtcattcat cagctggact ggagacggat 1380
gggagtttaa gctcgccgac cccgatgagg tggcccgccg gtggggaaag aggaaaaata 1440
agcccaagat gaactacgag aagctgagcc ggggcttacg ctactattac gacaagaaca 1500
tcatccacaa gacgtcgggg aagcgctacg tgtaccgctt cgtgtgcgac ctccagaact 1560
tgctggggtt cacgcccgag gaactgcacg ccatcctggg cgtccagccc gacacggagg 1620
actgaggtcg ccgggaccac cctgagccgg ccccaggctc gtggactgag tgggaagccc 1680
atcctgacca gctgctccga ggacccagga aaggcaggat tgaaaatgtc caggaaagtg 1740
gccaagaagc agtggcctta ttgcatccca aaccacgcct cttgaccagg ctgcctccct 1800
tgtggcagca acggcacagc taattctact cacagtgctt ttaagtgaaa atggtcgaga 1860
aagaggcacc aggaagccgt cctggcgcct ggcagtccgt gggacgggat ggttctggct 1920
gtttgagatt ctcaaaggag cgagcatgtc gtggacacac acagactatt tttagatttt 1980
cttttgcctt ttgcaaccag gaacagcaaa tgcaaaaact ctttgagagg gtaggagggt 2040
gggaaggaaa caaccatgtc atttcagaag ttagtttgta tatattataa taatcttata 2100
attgttctca gaatccctta acagttgtat ttaacagaaa ttgtatattg taatttaaaa 2160

taattatata actgtatttg aaataagaat tcagacatct gaggttttat ttcatttttc 2220
aatagcacat atggaatttt gcaaagattt aatctgccaa gggccgacta agagaagttg 2280
taaagtatgt attatttaca tttaatagac ttacagggat aaggcctgtg gggggtaatc 2340
cctgcttttt gtgttttttt gtttgtttgt ttgtttgttt ttgggggttt ttcttgcctt 2400
ggttgtctgg caaggacttt gtacatttgg gagtttttat gagaaactta aatgttatta 2460
tctgggctta tatctggcct ctgctttctc ctttaattgt aaagtaaaag ctataaagca 2520
gtatttttct tgacaaatgg catatgtttt ccacttcttt gcatgcgttt aagtcagttt 2580
atacacaaaa tggattttat tttttagttt aactgtgttt ctccgacagc tcacctctct 2640
ctgaccaccc agccatttcc ttcctgtgct ccacgttctt ctgtgtgatt aaaataagaa 2700
tattattttt ggaaatatgc aactcctttt cagagatcag gagggattta tgtagcagct 2760
atttttactg caaaagtaat tcactgggaa aaaaaatgta atttgtaaga aagctttatt 2820
tttatctcag ctctatgtaa agttaaagtt actgtacaga gctgaaggac ggggggcggt 2880
aggggtcttg atgaaacctc ttgaacgaag cacagtttgt cccatctttg ttcactcgtg 2940
tgtctcaacc atcttaatag catgctgctc ctttttgctc agtgtccaca gcaagatgac 3000
gtgattctta ttttcttgga cacagactat tctgaggcac agagcgggga cttaagatgg 3060
gaaagagaaa gcatcggagc cattcattcg gagaaaacgt tttgatcaaa atggagactt 3120
ttgtagtcgt ttcaaaagag cacctgagtc atgtgtattc ccggccttta taaatgaccc 3180
ggtcaagttg gtttcaaagt ccgacaggct tgtctgttta ctagctgcgt ggccttggac 3240
gggtggctga catctgtaaa gaatcctcct gtgatgaaac tgaggaatcg ggtggccggg 3300
caagctggga agagcaaagc cagagctgcg ctgcctcaat acccacaaaa gaccattccc 3360
agtatacata agcacaggat gtttttctca agagggatgt atttatcact tggacatctg 3420
tttataatat aaacagacat gtgactggga acatcttgct gccaaaagaa tcctaggcag 3480
tggctcattg tatgtgaggt tgaaccacgt gaaattgcca atattaggct ggcttttatc 3540
tacaaagaag gagtttcatg gggttcagcc taacagttat ggaaactaca gtccttataa 3600
accattggca tggtaataaa cagatcttaa gtataaaaat tttgtaattg ggcctttact 3660
ctctcaataa taaagtattt tgtttatata aaaaa 3695

<210> 18
<211> 1535
<212> DNA
<213> Homo sapiens

<400> 18
attaattctg gctccacttg ttgctcggcc caggttgggg agaggacgga gggtggccgc 60
agcgggttcc tgagtgaatt acccaggagg gactgagcac agcaccaact agagaggggt 120
caggggggtgc gggactcgag cgagcaggaa ggaggcagcg cctggcacca gggctttgac 180
tcaacagaat tgagacacgt ttgtaatcgc tggcgtgccc cgcgcacagg atcccagcga 240
aaatcagatt tcctggtgag gttgcgtggg tggattaatt tggaaaaaga aactgcctat 300
atcttgccat caaaaaactc acggaggaga agcgcagtca atcaacagta aacttaagag 360
acccccgatg ctcccctggt ttaacttgta tgcttgaaaa ttatctgaga gggaataaac 420
atcttttcct tcttccctct ccagaagtcc attggaatat taagcccagg agttgctttg 480
gggatggctg gaagtgcaat gtcttccaag ttcttcctag tggctttggc catatttttc 540
tccttcgccc aggttgtaat tgaagccaat tcttggtggt cgctaggtat gaataaccct 600
gttcagatgt cagaagtata tattatagga gcacagcctc tctgcagcca actggcagga 660
ctttctcaag gacagaagaa actgtgccac ttgtatcagg accacatgca gtacatcgga 720
gaaggcgcga agacaggcat caaagaatgc cagtatcaat tccgacatcg acggtggaac 780
tgcagcactg tggataacac ctctgttttt ggcagggtga tgcagatagg cagccgcgag 840
acggccttca catacgccgt gagcgcagca ggggtggtga acgccatgag ccgggcgtgc 900
cgcgagggcg agctgtccac ctgcggctgc agccgcgccg cgcgccccaa ggacctgccg 960
cgggactggc tctggggcgg ctgcggcgac aacatcgact atggctaccg ctttgccaag 1020
gagttcgtgg acgcccgcga gcgggagcgc atccacgcca agggctccta cgagagtgct 1080
cgcatcctca tgaacctgca caacaacgag gccggccgca ggacggtgta caacctggct 1140
gatgtggcct gcaagtgcca tggggtgtcc ggctcatgta gcctgaagac atgctggctg 1200
cagctggcag acttccgcaa ggtgggtgat gccctgaagg agaagtacga cacactggtt 1260
taaaaaacaa acatcgaaag gcttatgcca aatggaagat agaatataaa ataaaacgtt 1320
acttgtatat tggtaagtgg tttcaattgt ccttcagata attcatgtgg agatttttgg 1380
agaaaccatg acggatagtt taggatgact acatgtcaaa gtaataaaag agtggtgaat 1440
tttaccaaaa ccaagctatt tggaagcttc aaaaggtttc tatatgtaat ggaacaaaag 1500
gggaattctc ttttcctata tatgttcctt acaaa 1535

<210> 19
<211> 3877
<212> DNA
<213> Homo sapiens

<400> 19
cattagatct ttacatgaaa gtaaaattta taagatttct agaaagtcaa aagatgataa 60
ctatttctta ggatactaaa agcactcaca ttatagaaaa aaaatcagtt aactatactc 120
cacaaacatt aaaggctccc tataaaaaaa catttttaat aggcaagcca cagaaagggc 180
aaatattaat agtttgcaat acatatgtat gaaaaggaat tgaatctaga atatttaaca 240
aagctttaca actcaaaaaa tacaaagaaa atatttttct tccaattggc aaattactta 300
aacagaacct tcacaaaaga agataagaat gtttaataaa catttgaagc cataataatg 360
acatcattag ccatgatgga aatgcaaatt taagtaccac ttcacatcca caagaaaaag 420
ataaaaataa aaggactgag ctcaccaaac attggtgagg atgtggtaat actgaaattc 480
ttgtaccgtg ctcctgaggg tataacatat tacaggattt ttttgaaaac tagtggttcc 540
ttataaactt aatgccctgg caacctcaca cctatttact taagaatgaa agggccccgc 600
cctcctccct cctcgctcgc gggccgggcc cggcatggtg cggcgtcgcc gccgatggcg 660
ctgaggcgga gcatggggcg gccggggctc ccgccgctgc cgctgccgcc gccaccgcgg 720
ctcgggctgc tgctggcgga gtccgccgcc gcaggtctga agctcatggg agccccggtg 780
aagctgacag tgtctcaggg gcagccggtg aagctcaact gcagtgtgga ggggatggag 840
gagcctgaca tccagtgggt gaaggatggg gctgtggtcc agaacttgga ccagttgtac 900
atcccagtca gcgagcagca ctggatcggc ttcctcagcc tgaagtcagt ggagcgctct 960
gacgccggcc ggtactggtg ccaggtggag gatgggggtg aaaccgagat ctcccagcca 1020
gtgtggctca cggtagaagg tgtgccattt ttcacagtgg agccaaaaga tctggcagtg 1080
ccacccaatg ccccttttcca actgtcttgt gaggctgtgg gtccccctga acctgttacc 1140
attgtctggt ggagaggaac tacgaagatc gggggacccg ctccctctcc atctgtttta 1200
aatgtaacag gggtgaccca gagcaccatg ttttcctgtg aagctcacaa cctaaaaggc 1260
ctggcctctt ctcgcacagc cactgttcac cttcaagcac tgcctgcagc ccccttcaac 1320
atcaccgtga caaagctttc cagcagcaac gctagtgtgg cctggatgcc aggtgctgat 1380
ggccgagctc tgctacagtc ctgtacagtt caggtgacac aggccccagg aggctgggaa 1440
gtcctggctg ttgtggtccc tgtgcccccc tttacctgcc tgctccggga cctggtgcct 1500
gccaccaact acagcctcag ggtgcgctgt gccaatgcct tggggccctc tccctatgct 1560
gactgggtgc cctttcagac caagggtcta gccccagcca gcgctcccca aaacctccat 1620
gccatccgca cagattcagg cctcatcttg gagtgggaag aagtgatccc cgaggccctt 1680
ttggaaggcc ccctgggacc ctacaaactg tcctgggttc aagacaatgg aacccaggat 1740
gagctgacag tggaggggac cagggccaat ttgacaggct gggatcccca aaaggacctg 1800
atcgtacgtg tgtgcgtctc caatgcagtt ggctgtggac cctggagtca gccactggtg 1860
gtctcttctc atgaccgtgc aggccagcag ggccctcctc acagccgcac atcctgggta 1920
cctgtggtcc ttggtgtgct aacggccctg gtgacggctg ctgccctggc cctcatcctg 1980
cttcgaaaga gacggaaaga gacgcggttt gggcaagcct ttgacagtgt catggcccgg 2040
ggagagccag ccgttcactt ccgggcagcc cggtccttca atcgagaaag gcccgagcgc 2100
atcgaggcca cattggacag cttgggcatc agcgatgaac taaaggaaaa actggaggat 2160
gtgctcatcc cagagcagca gttcaccctg ggccggatgt tgggcaaagg agagtttggt 2220
tcagtgcggg aggcccagct gaagcaagag gatggctcct ttgtgaaagt ggctgtgaag 2280
atgctgaaag ctgacatcat tgcctcaagc gacattgaag agttcctcag ggaagcagct 2340
tgcatgaagg agtttgacca tccacacgtg gccaaacttg ttggggtaag cctccggagc 2400
agggctaaag gccgtctccc catccccatg gtcatcttgc ccttcatgaa gcatggggac 2460
ctgcatgcct tcctgctcgc ctcccggatt ggggagaacc cctttaacct acccctccag 2520
accctgatcc ggttcatggt ggacattgcc tgcggcatgg agtacctgag ctctcggaac 2580
ttcatccacc gagacctggc tgctcggaat tgcatgctgg cagaggacat gacagtgtgt 2640
gtggctgact tcggactctc ccggaagatc tacagtgact gtcggtacat actcaccccc 2700
ggagggctgg ctgagcagcc agggcaggca gagcaccagc cagagagtcc cctcaatgag 2760
acacagaggc ttttgctgct gcagcaaggg ctactgccac acagtagctg ttagcccaca 2820
ggcagagggc atcggggcca tttggccggc tctggtggcc actgagctgg ctgactaagc 2880
cccgtctgac cccagcccag acagcaaggt gtggaggctc ctgtggtagt cctcccaagc 2940
tgtgctggga agcccggact gaccaaatca cccaatccca gttcttcctg caaccactct 3000
gtggccagcc tggcatcagt ttaggccttg gcttgatgga agtgggccag tcctggttgt 3060
ctgaacccag gcagctggca ggagtggggt ggttatgttt ccatggttac catgggtgtg 3120
gatggcagtg tggggagggc aggtccagct ctgtgggccc taccctcctg ctgagctgcc 3180
cctgctgctt aagtgcatgc attgagctgc ctccagcctg gtggcccagc tattaccaca 3240

cttggggttt aaatatccag gtgtgcccct ccaagtcaca aagagatgtc cttgtaatat 3300
tccctttag gtgagggttg gtaaggggtt ggtatctcag gtctgaatct tcaccatctt 3360
tctgattccg caccctgcct acgccaggag aagttgaggg gagcatgctt ccctgcagct 3420
gaccgggtca cacaaaggca tgctggagta cccagcctat caggtgcccc tcttccaaag 3480
gcagcgtgcc gagccagcaa gaggaagggg tgctgtgagg cttgcccagg agcaagtgag 3540
gccggagagg agttcaggaa cccttctcca tacccacaat ctgagcacgc taccaaatct 3600
caaaatatcc taagactaac aaaggcagct gtgtctgagc ccaacccttc taaacggtga 3660
cctttagtgc caacttcccc tctaactgga cagcctcttc tgtcccaagt ctccagagag 3720
aaatcaggcc tgatgagggg gaattcctgg aacctggacc ccagccttgg tgggggagcc 3780
tctggaatgc atggggcggg tcctagctgt tagggacatt tccaagctgt tagttgctgt 3840
ttaaaataga aataaaattg aagactaaag acctaaa 3877

<210> 20
<211> 3532
<212> DNA
<213> Homo sapiens

<400> 20
ttcccctccc ctccccaccc ccttttttcg ctgctctccc gcttccccgc caatggagaa 60
gcgagctgat gacaaatagc gggccgcgga gtccgcggga cttcgcacca ggagtaataa 120
aacagaccca gagatcaagg agctggggag ggggcggggg aacagggagg gagagcgtgt 180
gagcgtctgc gagtgtgtgg aggcggctgc tgtggcagcg caggcggctc ggctccggcc 240
cggagcgcag cggaagccgc gagggatgca gcggcgggga ccttggccgg tggaggatgt 300
ggaggtggaa gtggagcgga tggcgctccc caagagctcc gccacgcgag gtttcgggct 360
cgtggttttg cttcctccgg ccaaggtccc cgccgctgca tccctcgcgg cttcccgtgc 420
gctccgggcc ggagccgagc cgcctgcgct gccacagcca gcgcctccac acactcgcag 480
acgctcacac gctctccctc cctgttcccc cgccccctcc ccagctcctt gatctctggg 540
tctgttttat tactcctggt gcgagtcccg cggactccgg cccgctattt gtcatcagct 600
cgctctccat tggcggggag cggagagcag cgaagaaggg ggtggggagg ggaggggaag 660
ggaaggggt ggaaactgcc tggagccgtt tctcgcgccg ctgttggtgc tgccgctgcc 720
tcctcctcct ccgccgccgc cgccgccgcc gccgccgcct cctccggctc ttcgctcggc 780
ccctctccgc ctccatgtgc cggatagcgg gagcgctgcg gaccctgctg ccgctgctgg 840
cggccctgct tcaggcgtct gtagaggctt ctggtgaaat cgcattatgc aagactggat 900
ttcctgaaga tgtttacagt gcagtcttat cgaaggatgt gcatgaagga cagcctcttc 960
tcaatgtgaa gtttagcaac tgcaatggaa aaagaaaagt acaatatgag agcagtgagc 1020
ctgcagattt taaggtggat gaagatggca tggtgtatgc cgtgagaagc tttccactct 1080
cttctgagca tgccaagttc ctgatatatg cccaagacaa agagacccag gaaaagtggc 1140
aagtggcagt aaaattgagc ctgaagccaa ccttaactga ggagtcagtg aaggagtcag 1200
cagaagttga agaaatagtg ttcccaagac aattcagtaa gcacagtggc cacctacaaa 1260
ggcagaagag agactgggtc atccctccaa tcaacttgcc agaaaactcc aggggacctt 1320
ttcctcaaga gcttgtcagg atcaggtctg atagagataa aaacctttca ctgcggtaca 1380
gtgtaactgg gccaggagct gaccagcctc caactggtat cttcattatc aaccccatct 1440
cgggtcagct gtcggtgaca aagcccctgg atcgcgagca gatagcccgg tttcatttga 1500
gggcacatgc agtagatatt aatggaaatc aagtggagaa ccccattgac attgtcatca 1560
atgttattga catgaatgac aacagacctg agttcttaca ccaggtttgg aatgggacag 1620
ttcctgaggg atcaaagcct ggaacatatg tgatgaccgt aacagcaatt gatgctgacg 1680
atcccaatgc cctcaatggg atgttgaggt acagaatcgt gtctcaggct ccaagcaccc 1740
cttcacccaa catgtttaca atcaacaatg agactggtga catcatcaca gtggcagctg 1800
gacttgatcg agaaaaagtg caacagtata cgttaataat tcaagctaca gacatggaag 1860
gcaatcccac atatggcctt tcaaacacag ccacggccgt catcacagtg acagatgtca 1920
atgacaatcc tccagagttt actgccatga cgttttatgg tgaagttcct gagaacaggg 1980
tagacatcat agtagctaat ctaactgtga ccgataagga tcaaccccat acaccagcct 2040
ggaacgcagt gtacagaatc agtggcggag atcctactgg acggttcgcc atccagaccg 2100
acccaaacag caacgacggg ttagtcaccg tggtcaaacc aatcgacttt gaaacaaata 2160
ggatgtttgt ccttactgtt gctgcagaaa atcaagtgcc attagccaag ggaattcagc 2220
acccgcctca gtcaactgca accgtgtctg ttacagttat tgacgtaaat gaaaaccctt 2280
attttgcccc caatcctaag atcattcgcc aagaagaagg gcttcatgcc ggtaccatgt 2340
tgacaacatt cactgctcag gacccagatc gatatatgca gcaaaatatt agatacacta 2400
aattatctga tcctgccaat tggctaaaaa tagatcctgt gaatggacaa ataactacaa 2460
ttgctgtttt ggaccgagaa tcaccaaatg tgaaaaacaa tatatataat gctactttcc 2520

ttgcttctga caatggaatt cctcctatga gtggaacagg aacgctgcag atctatttac 2580
ttgatattaa tgacaatgcc cctcaagtgt tacctcaaga ggcagagact tgcgaaactc 2640
cagaccccaa ttcaattaat attacagcac ttgattatga cattgatcca aatgctggac 2700
catttgcttt tgatcttcct ttatctccag tgactattaa gagaaattgg accatcactc 2760
ggcttaatgg tgattttgct cagcttaatt taaagataaa atttcttgaa gctggtatct 2820
atgaagttcc catcataatc acagattcgg gtaatcctcc caaatcaaat atttccatcc 2880
tgcgcgtgaa ggtttgccag tgtgactcca acggggactg cacagatgtg gacaggattg 2940
tgggtgcggg gcttggcacc ggtgccatca ttgccatcct gctctgcatc atcatcctgc 3000
ttatccttgt gctgatgttt gtggtatgga tgaaacgccg ggataaagaa cgccaggcca 3060
aacaactttt aattgatcca gaagatgatg taagagataa tattttaaaa tatgatgaag 3120
aaggtggagg agaagaagac caggactatg acttgagcca gctgcagcag cctgacactg 3180
tggagcctga tgccatcaag cctgtgggaa tccgacgaat ggatgaaaga cccatccacg 3240
ccgagcccca gtatccggtc cgatctgcag ccccacaccc tggagacatt ggggacttca 3300
ttaatgagaa aacctggccc atacagagct tacacctatg accttggctt cgtgggcacc 3360
atgatttcag caatgcatct atcatgcctg cctttggacc taatgagtat gaaccacatt 3420
acatcagaga agagtgccag ggtcaacaat taatatttta gagttacaac tacatgtgaa 3480
cctatgtact tgcattttca gcaatattgc agcatagtat tatttatctc ta 3532

<210> 21
<211> 3069
<212> DNA
<213> Homo sapiens

<400> 21
agattatgat cgcctgaggc ccctctccta cccagatacc gatgttatac tgatgtgttt 60
ttccttttt ttttttttt tttaagtaat taagggtagt taaattattt aaagtataca 120
aagtccaaac agccaggggt aaggtctcca agaggccttc ccagggtaag ggagtgcgga 180
gaggccccgg tcgccacccg cggtgcccat ggagcgggtg aagatgatca acgtgcagcg 240
tctgctggag gctgccgagt ttttggagcg ccgggagcga gagtgtgaac atggctacgc 300
ctcttcattc ccgtccatgc cgagcccccg actgcagcat tcaaagcccc cacggaggtt 360
gagccgggca cagaaacaca gcagcgggag cagcaacacc agcactgcca acagatctac 420
acacaatgag ctggaaaaga atcgcttgaa gaattggttg gttgggagaa gggataccag 480
aggcatgaag atgcttttga aggctattgc agtaatctag acgagctcat ctgcgccttt 540
gtttagaacg cttaaaagtt ctgattccac taggaccaga ctgcacccgg cacacaacac 600
ttggtttgct caacaaagcc aaagcacaca tcaagaaact tgaagaagct gaaagaaaaa 660
gccagcacca gctcgagaat ttggaacgag aacagagatt tttaaagtgg cgactggaac 720
agctgcaggg tcctcaggag atggaacgaa tacgaatgga cagcattgga tcaactattt 780
cttcagatcg ttctgattca gagcgagagg agattgaagt ggatgttgaa agcacagagt 840
tctcccatgg agaagtggac aatataagta ccaccagcat cagtgacatt gatgaccaca 900
gcagcctgcc gagtattggg agtgacgagg gttactccag tgccagtgtc aaactttcat 960
tcacttcata gaacccagca tgacataaca gtgcagggca aaatattcac tgggccaatt 1020
caatacaaac aatctcttaa attgggttca tgatgcagtc tcctctttaa aacaaaacaa 1080
aacaaaacaa aactatactt gaacaaaagg gtcagaggac ctgtatttaa gcaaatactt 1140
agcaaaaagt ggggcagagc tcccaaggag aacaaatatt cagaatattc atattggaaa 1200
aatcacaatt tttaatggca gcagaaaact tgtgtgaaat tttcttgatt tgagttgatt 1260
gagaagagga cattggagat gccatcctct ttctcttttc tagtttgctc atactacatt 1320
gagtagacac atttaaggat ggggttatga acccttcctg agctttatgg tcctaaaagc 1380
aaaataaaaa ctattcgaat gaaaagacaa gaaaatcagg tattaatctt ggatagctaa 1440
taatgagcta ttaaaactca gcctgggaca gtttatcatg aagcctgtgg atgatcaatc 1500
ctttattatt attttttttt ttttgaaaaa agctcatttc atgctctgca aaaggagaga 1560
ctcccatgaa gccttttgaa agggatcatc atgcagctca actttctgtt ggattccatg 1620
ctaagcaagc taaccttatc ctgcattgtt agcactaggc acccagctgc cacctctcca 1680
tcctgctgcc cttaggccac atgggagcag tccatgcatg acagcctcta tcctacaagg 1740
cctatgagta tggattgggg gggccaaaag gaaaaagctc catgtgcctc tttgtctgcg 1800
tgggtcagaa gagttgtgca cgcagattag caggccaagg tctgagccac agcagcattt 1860
ttatttcaga ttttgataac tgtttatatg tgttgaaaac caaaatgaca tctttttaaa 1920
gcttatccat aaaaaaaaat agatgtcttt tatagtggaa aaacacatgg ggaaaaaaat 1980
catctatttt gatgcagcat ttgataatga taaaacacct cacacctcac tctttatagt 2040
gcacaaaatg aatgaggtct gggctaggta gaaaaagggt caatgctatt tttgttttta 2100
gaatcattac cttttaccag cttttaacca tctgatatct atagtagaca cactatcata 2160

gttaacatag ttaagttcag cacttgtctc attttaatgt aaagatttgc ttccattttc 2220
ctacaggcag tctctctctt cctcacagtc ccactgtgca ggtgctattg ttactcttac 2280
gaatattttc agtaatgtta ttttcttcta agtgaaattt ctagcctgca ctttgatgtc 2340
atgtgttccc tttgtctttc aaactccaag gttcccctgt ggccctctcc cttaccctgg 2400
gaaggcctct tggagacctt acccctggct gtttggactt tgtatacttt aaataattta 2460
actaccctta attacttaaa aaaaaaaaaa aaagctttat gattttcata acttattgct 2520
gattttaatg gattgttaat ttcagtcctg tagttttatt ttatgtttag atagggctgg 2580
gcaaggaaaa agaaaataaa gacaaccata tttagcagtg cagttgagtt gtgtgttaat 2640
gttagactat ccctttgtga gtgacacttt aacagcattc actgcttcta tatatagtgt 2700
accatcttgg tcatacatta cgcctcaaca tatacttgtg ctcttccttt gcctccagaa 2760
gaagtttttc cttgattgtg ctatgtttca gtggaagaaa ttctttgaag tagatgtgag 2820
tgaaaaactg catgccttta gaagcccagt atcagaactt gctacgtttc aggtgctagg 2880
gacttaatga aaaacaggac aaaacaattc ctttttgtgg cccaggtaaa ttatttctgg 2940
tttcacttat aattactaat ggctgagtca agatgttgtc tctgtgtttg cttactcttg 3000
atcaagtgtg agacagtttg aagactgtgc taccatacaa agtgaatgaa gccagtgact 3060
aagaaacaa 3069

<210> 22
<211> 2971
<212> DNA
<213> Homo sapiens

<400> 22
cggccgcgca aggaggcgcg ctgcgagggc gcggggctgg cccccgccgc gcccccggct 60
gtgccccccg ccgtggccgc gccccagccc ccggccctgc ccgaggaccc cgctggggcc 120
aagcccaggt gcccccttctc agacattttc aacaccagcg agaactcgat ggagaagcac 180
atcaacactt ttctgcagaa cgtgcagatt ctgctcgagg ccgccagcta cctggagcag 240
atcgagaaag aaaacaaaaa gtgtgaacat ggctacgcct cttcattccc gtccatgccg 300
agcccccgac tgcagcattc aaagccccca cggaggttga gccgggcaca gaaacacagc 360
agcgggagca gcaacaccag cactgccaac agatctacac acaatgagct ggaaaagaat 420
cgacgagctc atctgcgcct ttgtttagaa cgcttaaaag ttctgattcc actaggacca 480
gactgcaccc ggcacacaac acttggtttg ctcaacaaag ccaaagcaca catcaagaaa 540
cttgaagaag ctgaaagaaa aagccagcac cagctcgaga atttggaacg agaacagaga 600
tttttaaagt ggcgactgga acagctgcag ggtcctcagg agatggaacg aatacgaatg 660
gacagcattg gatcaactat ttcttcagat cgttctgatt cagagcgaga ggagattgaa 720
gtggatgttg aaagcacaga gttctcccat ggagaagtgg acaatataag taccaccagc 780
atcagtgaca ttgatgacca cagcagcctg ccgagtattg ggagtgacga gggttactcc 840
agtgccagtg tcaaactttc attcacttca tagaacccag catgacataa cagtgcaggg 900
caaaatattc actgggccaa ttcaatacaa acaatctctt aaattgggtt catgatgcag 960
tctcctcttt aaaacaaaac aaaacaaaac aaaactatac ttgaacaaaa gggtcagagg 1020
acctgtattt aagcaaatac ttagcaaaaa gtggggcaga gctcccaagg agaacaaata 1080
ttcagaatat tcatattgga aaaatcacaa tttttaatgg cagcagaaaa cttgtgtgaa 1140
attttcttga tttgagttga ttgagaagag gacattggag atgccatcct ctttctcttt 1200
tctagtttgc tcatactaca ttgagtagac acatttaagg atggggttat gaacccttcc 1260
tgagctttat ggtcctaaaa gcaaaataaa aactattcga atgaaaagac aagaaaatca 1320
ggtattaatc ttggatagct aataatgagc tattaaaact cagcctggga cagtttatca 1380
tgaagcctgt ggatgatcaa tcctttatta ttatttttt ttttttgaaa aaagctcatt 1440
tcatgctctg caaaaggaga gactcccatg aagccttttg aaagggatca tcatgcagct 1500
caactttctg ttggattcca tgctaagcaa gctaacctta tcctgcattg ttagcactag 1560
gcacccagct gccacctctc catcctgctg cccttaggcc acatgggagc agtccatgca 1620
tgacagcctc tatcctacaa ggcctatgag tatggattgg gggggccaaa aggaaaaagc 1680
tccatgtgcc tctttgtctg cgtgggtcag aagagttgtg cacgcagatt agcaggccaa 1740
ggtctgagcc acagcagcat ttttatttca gattttgata actgtttata tgtgttgaaa 1800
accaaaatga catctttta aagcttatcc ataaaaaaaa atagatgtct tttatagtgg 1860
aaaaacacat ggggaaaaaa atcatctatt ttgatgcagc atttgataat gataaaacac 1920
ctcacacctc actctttata gtgcacaaaa tgaatgaggt ctgggctagg tagaaaaagg 1980
gtcaatgcta tttttgtttt tagaatcatt acctttttacc agcttttaac catctgatat 2040
ctatagtaga cacactatca tagttaacat agttaagttc agcacttgtc tcattttaat 2100
gtaaagattt gcttccattt tcctacaggc agtctctctc ttcctcacag tcccactgtg 2160
caggtgctat tgttactctt acgaatattt tcagtaatgt tattttcttc taagtgaaat 2220

ttctagcctg cactttgatg tcatgtgttc cctttgtctt tcaaactcca aggttcccct 2280
gtggccctct cccttaccct gggaaggcct cttggagacc ttacccctgg ctgtttggac 2340
tttgtatact ttaaataatt taactaccct taattactta aaaaaaaaaa aaaaagcttt 2400
atgattttca taacttattg ctgattttaa tggattgtta atttcagtcc tgtagtttta 2460
ttttatgttt agatagggct gggcaaggaa aaagaaaata aagacaacca tatttagcag 2520
tgcagttgag ttgtgtgtta atgttagact atccctttgt gagtgacact ttaacagcat 2580
tcactgcttc tatatatagt gtaccatctt ggtcatacat tacgcctcaa catatacttg 2640
tgctcttcct ttgcctccag aagaagtttt tccttgattg tgctatgttt cagtggaaga 2700
aattctttga agtagatgtg agtgaaaaac tgcatgcctt tagaagccca gtatcagaac 2760
ttgctacgtt tcaggtgcta gggacttaat gaaaaacagg acaaaacaat tccttttttgt 2820
ggcccaggta aattatttct ggtttcactt ataattacta atggctgagt caagatgttg 2880
tctctgtgtt tgcttactct tgatcaagtg tgagacagtt tgaagactgt gctaccatac 2940
aaagtgaatg aagccagtga ctaagaaaca a 2971

<210> 23
<211> 1394
<212> DNA
<213> Homo sapiens

<400> 23
actcactata gggctcgagc ggccgcccgg gcaggtgtct gcccgcagcc atgagcgtgc 60
tcggccccgs tsgagyccry wgtsctctaa wkagtctcca ccgccgtcca ggacccactt 120
gcagcatgga gtcgcccgcc tcgagccagc ccgccagcat gccccagtcc aaaggaaaat 180
ccaagaggaa gaaggatcta cggatatcct gcatgtccaa gccacccgca cccaacccca 240
caccccccg gaacctggac tcccggacct tcatcaccat tggagacaga aactttgagg 300
tggaggctga tgacttggtg accatctcag aactgggccg tggagcctat ggggtggtag 360
agaaggtgcg gcacgcccag agcggcacca tcatggccgt gaagcggatc cgggccaccg 420
tgaactcaca ggagcagaag cggctgctca tggacctgga catcaacatg cgcacggtcg 480
actgtttcta cactgtcacc ttctacgggg cactattcag agagggagac gtgtggatct 540
gcatggagct catggacaca tccttggaca agttctaccg gaaggtgctg gataaaaaca 600
tgacaattcc agaggacatc cttggggaga ttgctgtgtc tatcgtgcgg gccctggagc 660
atctgcacag caagctgtcg gtgatccaca gagatgtgaa gccctccaat gtccttatca 720
acaaggaggg ccatgtgaag atgtgtgact ttggcatcag tggctacttg gtggactctg 780
tggccaagac gatggatgcc ggctgcaagc cctacatggc ccctgagagg atcaacccag 840
agctgaacca gaagggctac aatgtcaagt ccgacgtctg gagcctgggc atcaccatga 900
ttgagatggc catcctgcgg ttcccttacg agtcctgggg gaccccgttc cagcagctga 960
agcaggtggt ggaggagccg tccccccagc tcccagccga ccgtttctcc cccgagtttg 1020
tggacttcac tgctcagtgc ctgaggaaga accccgcaga gcgtatgagc tacctggagc 1080
tgattggagc tgatcgcttc tcccccaccc cctagggtac cagcaggcag agccttgccc 1140
tctgctcagg ctggggtcca gtgggagggg cccaagatct ctgctcagag aagtgcaggg 1200
ggagccttcc agctcactct ccctgaggac tggcttgaca ggggctatgg gtttgctttg 1260
gtgttgtttt taaaaaaaga aaatatattt ttttgaaaaa acgactgccc atcccgggtc 1320
ctttccctga tgggttgggg cagttacctg gttgctgttt taattaaaaa ctttagagca 1380
caatggatct cgag 1394

<210> 24
<211> 1717
<212> DNA
<213> Homo sapiens

<400> 24
tcccttggcc ccaggagaca ggggttgcag aaagccgaga tcgtgccact gcactccatc 60
ctgggtgaga gagcaagacc ctgtctcaac aaaaaatttt taaaaaataa aataaataat 120
aatacagcaa aaagatttgc tttctcggct tcagtgtggg cggtaactcc atcgtgcaat 180
gagaaaggcg aatttcttcc agacaccaat cccggaggtc gcttctgttg ctaggctccc 240
agaaagcagg gttcggacgt cattgggagg cgaggctaga gcggggttgt gtgtggcgga 300
gggaggcggg gctggaggaa acgctcgttg ctaaggaacg cagcgctctt cccgctctgg 360
agaggcgcga ctgggcttgc gcagtgtcga cgccggcgcc ggcgcgccgg ggtttgaaag 420
gcccgagcct cgcgcgcttg cgcactttag ccagcgcagg gcgcaccccg ctccctccca 480

ctctccctgc ccctcggacc ccatactcta cctcatcctt ctggccaggc gaagcccacg 540
acgttgacat gccggagatc cgcctccgcc atgtcgtgtc ctgcagcagc caggactcga 600
ctcactgtgc agaaaatctt ctcaaggcag acacttaccg aaaatggcgg gcagccaagg 660
caggcgagaa gaccatctct gtggtcctac agttggagaa ggaggagcag atacacagtg 720
tggacattgg gaatgatggc tcagctttcg tggaggtgct ggtgggcagt tcagctggag 780
gcgctgggga gcaagactat gaggtccttc tggtcacctc atctttcatg tcccccttccg 840
agagccgcag tggctcaaac cccaaccgcg ttcgcatgtt tgggcctgac aagctggtcc 900
gggcagccgc cgagaagcgc tgggaccggg tcaaaattgt ttgcagccag ccctacagca 960
aggactcccc ctttggcttg agttttgtac ggtttcatag ccccccagac aaagatgagg 1020
cagaggcccc gtcccagaag gtgacagtga ccaagcttgg ccagttccgt gtgaaggagg 1080
aggatgagag cgccaactct ctgaggccgg gggctctctt cttcagccgg atcaacaaga 1140
catccccagt cacagccagc gacccggcag gacctagcta tgcagctgct accctccagg 1200
cttctagtgc tgcctcctca gcctctccag tctccagggc cataggcagc acctccaagc 1260
cccaggagtc tccctggcat tcgttcgtcc ccgatggatc tacagttgca atgagaagca 1320
gaagttactt cctcaccagc tctatggggt ggtgccgcaa gcctgaagta tgtgctatac 1380
acacacacac acacacacac acacacacac acacacgatg catttaataa agatgagttg 1440
gttctcatcc aagagtctcc caaaactcta agaggctccc tgggacctgg ggaagaatgc 1500
tgggcacctc cgtcagagat ctggtacaca aggaactctt tgtctcttct gcttggcccc 1560
ttatccctgt gttggcaaga ggcagggaac tgggaatctg accctcagca ctgcccctca 1620
acttttttctg gccctctgag ccacacctgt atcttggctg tccctttgtg gctggannnt 1680
gggtacccat gaggcttgtc tctctcctga agcctca 1717

<210> 25
<211> 1346
<212> DNA
<213> Homo sapiens

<400> 25
tcccttggcc ccaggagaca ggggttgcag aaagccgaga tcgtgccact gcactccatc 60
ctgggtgaga gagcaagacc ctgtctcaac aaaaaatttt taaaaaataa aataaataat 120
aatacagcaa aaagatttgc tttctcggct tcagtgtggg cggtaactcc atcgtgcaat 180
gagaaaggcg aatttcttcc agacaccaat cccggaggtc gcttctgttg ctaggctccc 240
agaaagcagg gttcggacgt cattgggagg cgaggctaga gcggggttgt gtgtggcgga 300
gggaggcggg gctggaggaa acgctcgttg ctaaggaacg cagcgctctt cccgctctgg 360
agaggcgcga ctgggcttgc gcagtgtcga cgccggcgcc ggcgcgccgg ggtttgaaag 420
gcccgagcct cgcgcgcttg cgcactttag ccagcgcagg gcgcaccccg ctccctccca 480
ctctccctgc ccctcggacc ccatactcta cctcatcctt ctggccaggc gaagcccacg 540
acgttgacat gccggagatc cgcctccgcc atgtcgtgtc ctgcagcagc caggactcga 600
ctcactgtgc agaaaatctt ctcaaggcag acacttaccg aaaatggcgg gcagccaagg 660
caggcgagaa gaccatctct gtggtcctac agttggagaa ggaggagcag atacacagtg 720
tggacattgg gaatgatggc tcagctttcg tggaggtgct ggtgggcagt tcagctggag 780
gcgctgggga gcaagactat gaggtccttc tggtcacctc atctttcatg tcccccttccg 840
agagccgcag tggctcaaac cccaaccgcg ttcgcatgtt tgggcctgac aagctggtcc 900
gggcagccgc cgagaagcgc tgggaccggg tcaaaattgt ttgcagccag ccctacagca 960
aggactcccc ctttggcttg agttttgtac ggtttcatag ccccccagac aaagatgagg 1020
cagaggcccc gtcccagaag gtgacagtga ccaagcttgg ccagttccgt gtgaaggagg 1080
aggatgagag cgccaactct ctgaggccgg gggctctctt cttcagccgg atcaacaaga 1140
catccccagt cacagccagc gacccggcag gacctagcta tgcagctgct accctccagg 1200
cttctagtgc tgcctcctca gcctctccag tctccagggc cataggcagc acctccaagc 1260
cccaggagtc atcagacttt ggtggggtgg aggaggagag aagctggagg cctcaatcca 1320
tccccatccc ctcagcccca gggagt 1346

<210> 26
<211> 1643
<212> DNA
<213> Homo sapiens

<400> 26
tcccttggcc ccaggagaca ggggttgcag aaagccgaga tcgtgccact gcactccatc 60

ctgggtgaga gagcaagacc ctgtctcaac aaaaaatttt taaaaaataa aataaataat 120
aatacagcaa aaagatttgc tttctcggct tcagtgtggg cggtaactcc atcgtgcaat 180
gagaaaggcg aatttcttcc agacaccaat cccggaggtc gcttctgttg ctaggctccc 240
agaaagcagg gttcggacgt cattgggagg cgaggctaga gcggggttgt gtgtggcgga 300
gggaggcggg gctggaggaa acgctcgttg ctaaggaacg cagcgctctt cccgctctgg 360
agaggcgcga ctgggcttgc gcagtgtcga cgccggcgcc ggcgcgccgg ggtttgaaag 420
gcccgagcct cgcgcgcttg cgcactttag ccagcgcagg gcgcaccccg ctccctccca 480
ctctccctgc ccctcggacc ccatactcta cctcatcctt ctggccaggc gaagcccacg 540
acgttgacat gccggagatc cgcctccgcc atgtcgtgtc ctgcagcagc caggactcga 600
ctcactgtgc agaaaatctt ctcaaggcag acacttaccg aaaatggcgg gcagccaagg 660
caggcgagaa gaccatctct gtggtcctac agttggagaa ggaggagcag atacacagtg 720
tggacattgg gaatgatggc tcagctttcg tggaggtgct ggtgggcagt tcagctggag 780
gcgctgggga gcaagactat gaggtccttc tggtcacctc atctttcatg tccccttccg 840
agagccgcag tggctcaaac cccaaccgcg ttcgcatgtt tgggcctgac aagctggtcc 900
gggcagccgc cgagaagcgc tgggaccggg tcaaaattgt ttgcagccag ccctacagca 960
aggactcccc ctttggcttg agttttgtac ggtttcatag ccccccagac aaagatgagg 1020
cagaggcccc gtcccagaag gtgacagtga ccaagcttgg ccagttccgt gtgaaggagg 1080
aggatgagag cgccaactct ctgaggctcg aggactatat gagtgaccgg gttcagtttg 1140
tgatcacagc acaggaatgg gatcccagct ttgaggaggc cctgatggac aacccctccc 1200
tggcattcgt tcgtccccga tggatctaca gttgcaatga gaagcagaag ttacttcctc 1260
accagctcta tggggtggtg ccgcaagcct gaagtatgtg ctatacacac acacacacac 1320
acacacacac acacacacac acgatgcatt taataaagat gagttggttc tcatccaaga 1380
gtctcccaaa actctaagag gctccctggg acctggggaa gaatgctggg cacctccgtc 1440
agagatctgg tacacaagga actctttgtc tcttctgctt ggccccttat ccctgtgttg 1500
gcaagaggca gggaactggg aatctgaccc tcagcactgc ccctcaactt tttctggccc 1560
tctgagccac acctgtatct tggctgtccc tttgtggctg gannntgggt acccatgagg 1620
cttgtctctc tcctgaagcc tca 1643

<210> 27
<211> 2713
<212> DNA
<213> Homo sapiens

<400> 27
tcccttggcc ccaggagaca ggggttgcag aaagccgaga tcgtgccact gcactccatc 60
ctgggtgaga gagcaagacc ctgtctcaac aaaaaatttt taaaaaataa aataaataat 120
aatacagcaa aaagatttgc tttctcggct tcagtgtggg cggtaactcc atcgtgcaat 180
gagaaaggcg aatttcttcc agacaccaat cccggaggtc gcttctgttg ctaggctccc 240
agaaagcagg gttcggacgt cattgggagg cgaggctaga gcggggttgt gtgtggcgga 300
gggaggcggg gctggaggaa acgctcgttg ctaaggaacg cagcgctctt cccgctctgg 360
agaggcgcga ctgggcttgc gcagtgtcga cgccggcgcc ggcgcgccgg ggtttgaaag 420
gcccgagcct cgcgcgcttg cgcactttag ccagcgcagg gcgcaccccg ctccctccca 480
ctctccctgc ccctcggacc ccatactcta cctcatcctt ctggccaggc gaagcccacg 540
acgttgacat gccggagatc cgcctccgcc atgtcgtgtc ctgcagcagc caggactcga 600
ctcactgtgc agaaaatctt ctcaaggcag acacttaccg aaaatggcgg gcagccaagg 660
caggcgagaa gaccatctct gtggtcctac agttggagaa ggaggagcag atacacagtg 720
tggacattgg gaatgatggc tcagctttcg tggaggtgct ggtgggcagt tcagctggag 780
gcgctgggga gcaagactat gaggtccttc tggtcacctc atctttcatg tccccttccg 840
agagccgcag tggctcaaac cccaaccgcg ttcgcatgtt tgggcctgac aagctggtcc 900
gggcagccgc cgagaagcgc tgggaccggg tcaaaattgt ttgcagccag ccctacagca 960
aggactcccc ctttggcttg agttttgtac ggtttcatag ccccccagac aaagatgagg 1020
cagaggcccc gtcccagaag gtgacagtga ccaagcttgg ccagttccgt gtgaaggagg 1080
aggatgagag cgccaactct ctgaggccgg gggctctctt cttcagccgg atcaacaaga 1140
catccccagt cacagccagc gacccggcag gacctagcta tgcagctgct accctccagg 1200
cttctagtgc tgcctcctca gcctctccag tctccagggc cataggcagc acctccaagc 1260
cccaggagtc tcccaaaggg aagaggaagt tggatttgaa ccaagaagaa aagaagaccc 1320
ccagcaaacc accagcccag ctgtcgccat ctgttcccaa gagacctaaa ttgccagctc 1380
caactcgtac cccagccaca gccccagtcc ctgcccgagc acaggggggca gtgacaggca 1440
aaccccgagg agaaggcacc gagcccagac gaccccgagc tggcccagag gagctgggga 1500
agatccttca gggtgtggta gtggtgctga gtggcttcca gaacccccttc cgctccgagc 1560

tgcgagataa ggccctagag cttggggcca agtatcggcc agactggacc cgggacagca 1620
cgcacctcat ctgtgccttt gccaacaccc ccaagtacag ccaggtccta ggcctgggag 1680
gccgcatcgt gcgtaaggag tgggtgctgg actgtcaccg catgcgtcgg cggctgccct 1740
cccggaggta cctcatggca gggccaggtt ccagcagtga ggaggatgag gcctctcaca 1800
gcggtggcag cggagatgaa gcccccaagc ttcctcagaa gcaaccccag accaaaacca 1860
agcccactca ggcagctgga cccagctcac cccagaagcc cccaacccct gaagagacca 1920
aagcagcctc accagtgctc caggaagata tagacattga gggggtacag tcagaaggac 1980
aggacaatgg ggcggaagat tctggggaca cagaggatga gctgaggagg gtggcagagc 2040
agaaggaaca cagactgccc cctggccagg aggagaatgg ggaagacccg tatgcaggct 2100
ccacggatga gaacacggac agtgaggaac accaggagcc tcctgatctg ccagtccctg 2160
agctccccag atttcttcca gggcaagcac ttctttcttt acggggagtt ccctggggac 2220
gagcggcgga aactcatccg atacgtcaca gccttcaatg gggagctccc tggcattcgt 2280
tcgtccccga tggatctaca gttgcaatga gaagcagaag ttacttcctc accagctcta 2340
tggggtggtg ccgcaagcct gaagtatgtg ctatacacac acacacacac acacacacac 2400
acacacacac acgatgcatt taataaagat gagttggttc tcatccaaga gtctcccaaa 2460
actctaagag gctccctggg acctggggaa gaatgctggg cacctccgtc agagatctgg 2520
tacacaagga actctttgtc tcttctgctt ggccccttat ccctgtgttg gcaagaggca 2580
gggaactggg aatctgaccc tcagcactgc ccctcaactt tttctggccc tctgagccac 2640
acctgtatct tggctgtccc tttgtggctg gannntgggt acccatgagg cttgtctctc 2700
tcctgaagcc tca 2713

<210> 28
<211> 2143
<212> DNA
<213> Homo sapiens

<400> 28
cggagtgccg ggtcgcgcct gcaccgaagg tcccggctcc tgtgccctcc ctgcagccgt 60
cagggaccgt cccccaactc ccctttccgc tcaggcaggg tcctcgcggc ccatgctggc 120
cgctggggac ccgcgcagcc cagaccgttc ccgggccggc cagccggcca ccatggtggc 180
cctgaggcct gtgcagcaac tccaggggggg ctaaagggct cagagtgcag gccgtggggc 240
gcgagggtcc cgggcctgag ccccgcgcca tggccggggc catcgcttcc cgcatgagct 300
tcagctctct caagaggaag caacccaaga cgttcaccgt gaggatcgtc accatggacg 360
ccgagatgga gttcaattgc gagatgaagt ggaaagggaa ggacctcttt gatttggtgt 420
gccggactct ggggctccga gaaacctggt tctttggact gcagtacaca atcaaggaca 480
cagtggcctg gctcaaaatg gacaagaagg tactggatca tgatgtttca aaggaagaac 540
cagtcacctt tcacttcttg gccaaatttt atcctgagaa tgctgaagag gagctggttc 600
aggagatcac acaacattta ttcttcttac aggtaaagaa gcagatttta gatgaaaaga 660
tctactgccc tcctgaggct tctgtgctcc tggcttctta cgccgtccag gccaagtatg 720
gtgactacga ccccagtgtt cacaagcggg gatttttggc ccaagaggaa ttgcttccaa 780
aaagggtaat aaatctgtat cagatgactc cggaaatgtg ggaggagaga attactgctt 840
ggtacgcaga gcaccgaggc cgagccaggg atgaagctga aatggaatat ctgaagatag 900
ctcaggacct ggagatgtac ggtgtgaact actttgcaat ccggaataaa aagggcacag 960
agctgctgct tggagtggat gccctggggc ttcacattta tgaccctgag aacagactga 1020
cccccaagat ctccttcccg tggaaaaaat gaaatccgaa acatctcgta cagtgacaag 1080
gagtttacta ttaaaccact ggataagaaa attgatgtct tcaagtttaa ctcctcaaag 1140
cttcgtgtta ataagctgat tctccagcta tgtatcggga accatgatct atttatgagg 1200
agaaggaaag ccgattcttt ggaagttcag cagatgaaag cccaggccag ggaggagaag 1260
gctagaaagc agatgaaaga agaagcaaca atggccaacg aagcactgat gcggtctgag 1320
gagacagctg acctgttggc tgaaaaggcc cagatcaccg aggaggaggc aaaacttctg 1380
gcccagaagg ccgcagaggc tgagcaggaa atgcagcgca tcaaggccac agcgattcgc 1440
acggaggagg agaagcgcct gatggagcag aaggtgctgg aagccgaggt gctggcactg 1500
aagatggctg aggagtcaga gaggagggcc aaagaggcag atcagctgaa gcaggacctg 1560
caggaagcac gcgaggcgga gcgaagagcc aagcagaagc tcctggagat tgccaccaag 1620
cccacgtacc cgcccatgaa cccaattcca gcaccgttgc ctcctgacat accaagcttc 1680
aacctcattg gtgacagcct gtctttcgac ttcaaagata ctgacatgaa gcggctttcc 1740
atggagatag agaaagaaaa agtggaatac atggaaaaga gcaagcatct gcaggagcag 1800
ctcaatgaac tcaagacaga aatcgaggcc ttgaaactga aagagaggga gacagctctg 1860
gatattctgc acaatgagaa ctccgacagg ggtggcagca gcaagcacaa taccattaaa 1920
aagctcacct tgcagagcgc caagtcccga gtggccttct ttgaagagct ctagcaggtg 1980

acccagccac cccaggacct gccacttctc ctgctaccgg gaccgcggga tggaccagat 2040
atcaagagag ccatccatag ggagctggct ggggggtttcc gtgggagctc cagaactttc 2100
cccagctgac atggaaatac aattgtctgc cggcctcccc tca 2143

<210> 29
<211> 540
<212> DNA
<213> Homo sapiens

<400> 29
gcgtagacgc gccgcgtccc cgcytgccgc tgctccgccg cagtcgccgc tccagtctat 60
ccggcactag gaacagcccc gagcggcgag acggtccccg ccatgtctgc ggccatgagg 120
gagaggttcg accggttcct gcacgagaag aactgcatga ctgaccttct ggccaagctc 180
gaggccaaaa ccggcgtgaa caggagcttc atcgctcttg gtgtcatcgg actggtggcc 240
ttgtacctgg tgttcggtta tggagcctct ctcctctgca acctgatagg atttggctac 300
ccagcctaca tctcaattaa agctatagag agtcccaaca aagaagatga tacccagtgg 360
ctgacctact gggtagtgta tggtgtgttc agcattgctg aattcttctc tgatatcttc 420
ctgtcatggt tccccttcta ctacatgctg aagcagattt atttagaacc tccatgtgcc 480
agattctgtt ctacatctgg gagatacttt ggcgaataaa acaaagtcct tgttgtcaaa 540

<210> 30
<211> 4533
<212> DNA
<213> Homo sapiens

<400> 30
cctactctat tcagatattc tccagattcc taaagattag agatcatttc tcattctcct 60
aggagtactc acttcaggaa gcaaccagat aaaagagagg tgcaacggaa gccagaacat 120
tcctcctgga aattcaacct gtttcgcagt ttctcgagga atcagcattc agtcaatccg 180
ggccgggagc agtcatctgt ggtgaggctg attggctggg caggaacagc gccggggcgt 240
gggctgagca cagcgcttcg ctctctttgc cacaggaagc ctgagctcat tcgagtagcg 300
gctcttccaa gctcaaagaa gcagaggccg ctgttcgttt cctttaggtc tttccactaa 360
agtcggagta tcttcttcca agatttcacg tcttggtggc cgttccaagg agcgcgaggt 420
cgggatggat cttgaagggg accgcaatgg aggagcaaag aagaagaact tttttaaact 480
gaacaataaa agtgaaaaag ataagaagga aaagaaacca actgtcagtg tattttcaat 540
gtttcgctat tcaaattggc ttgacaagtt gtatatggtg gtgggaactt tggctgccat 600
catccatggg gctggacttc ctctcatgat gctggtgttt ggagaaatga cagatatctt 660
tgcaaatgca ggaaatttag aagatctgat gtcaaacatc actaatagaa gtgatatcaa 720
tgatacaggg ttcttcatga atctggagga agacatgacc aggtatgcct attattacag 780
tggaattggt gctggggtgc tggttgctgc ttacattcag gtttcatttt ggtgcctggc 840
agctggaaga caaatacaca aaattagaaa acagtttttt catgctataa tgcgacagga 900
gataggctgg tttgatgtgc acgatgttgg ggagcttaac acccgactta cagatgatgt 960
ctctaagatt aatgaagtta ttggtgacaa aattggaatg ttctttcagt caatggcaac 1020
atttttcact gggtttatag taggatttac acgtggttgg aagctaaccc ttgtgatttt 1080
ggccatcagt cctgttcttg gactgtcagc tgctgtctgg gcaaagatac tatcttcatt 1140
tactgataaa gaactcttag cgtatgcaaa agctggagca gtagctgaag aggtcttggc 1200
agcaattaga actgtgattg catttggagg acaaaagaaa gaacttgaaa ggtacaacaa 1260
aaatttagaa gaagctaaaa gaattgggat aaagaaagct attacagcca atatttctat 1320
aggtgctgct ttcctgctga tctatgcatc ttatgctctg gccttctggt atgggaccac 1380
cttggtcctc tcaggggaat attctattgg acaagtactc actgtattct tttctgtatt 1440
aattggggct tttagtgttg gacaggcatc tccaagcatt gaagcatttg caaatgcaag 1500
aggagcagct tatgaaatct tcaagataat tgataataag ccaagtattg acagctattc 1560
gaagagtggg cacaaaccag ataatattaa gggaaatttg gaattcagaa atgttcactt 1620
cagttaccca tctcgaaaag aagttaagat cttgaagggc ctgaacctga aggtgcagag 1680
tgggcagacg gtggccctgg ttggaaacag tggctgtggg aagagcacaa cagtccagct 1740
gatgcagagg ctctatgacc ccacagaggg gatggtcagt gttgatggac aggatattag 1800
gaccataaat gtaaggtttc tacgggaaat cattggtgtg gtgagtcagg aacctgtatt 1860
gtttgccacc acgatagctg aaaacattcg ctatggccgt gaaaatgtca ccatggatga 1920
gattgagaaa gctgtcaagg aagccaatgc ctatgacttt atcatgaaac tgcctcataa 1980

atttgacacc ctggttggag agagaggggc ccagttgagt ggtgggcaga agcagaggat 2040
cgccattgca cgtgccctgg ttcgcaaccc caagatcctc ctgctggatg aggccacgtc 2100
agccttggac acagaaagcg aagcagtggt tcaggtggct ctggataagg ccagaaaagg 2160
tcggaccacc attgtgatag ctcatcgttt gtctacagtt cgtaatgctg acgtcatcgc 2220
tggtttcgat gatggagtca ttgtggagaa aggaaatcat gatgaactca tgaaagagaa 2280
aggcatttac ttcaaacttg tcacaatgca gacagcagga aatgaagttg aattagaaaa 2340
tgcagctgat gaatccaaaa gtgaaattga tgccttggaa atgtcttcaa atgattcaag 2400
atccagtcta ataagaaaaa gatcaactcg taggagtgtc cgtggatcac aagcccaaga 2460
cagaaagctt agtaccaaag aggctctgga tgaaagtata cctccagttt ccttttggag 2520
gattatgaag ctaaatttaa ctgaatggcc ttattttgtt gttggtgtat tttgtgccat 2580
tataaatgga ggcctgcaac cagcatttgc aataatattt tcaaagatta taggggtttt 2640
tacaagaatt gatgatcctg aaacaaaacg acagaatagt aacttgtttt cactattgtt 2700
tctagccctt ggaattattt cttttattac atttttcctt cagggtttca catttggcaa 2760
agctggagag atcctcacca agcggctccg atacatggtt ttccgatcca tgctcagaca 2820
ggatgtgagt tggtttgatg accctaaaaa caccactgga gcattgacta ccaggctcgc 2880
caatgatgct gctcaagtta aaggggctat aggttccagg cttgctgtaa ttacccagaa 2940
tatagcaaat cttgggacag gaataattat atccttcatc tatggttggc aactaacact 3000
gttactctta gcaattgtac ccatcattgc aatagcagga gttgttgaaa tgaaaatgtt 3060
gtctggacaa gcactgaaag ataagaaaga actagaaggt gctgggaaga tcgctactga 3120
agcaatagaa aacttccgaa ccgttgtttc tttgactcag gagcagaagt ttgaacatat 3180
gtatgctcag agtttgcagg taccatacag aaactctttg aggaaagcac acatctttgg 3240
aattacattt tccttcaccc aggcaatgat gtatttttcc tatgctggat gtttccggtt 3300
tggagcctac ttggtggcac ataaactcat gagctttgag gatgttctgt tagtattttc 3360
agctgttgtc tttggtgcca tggccgtggg gcaagtcagt tcatttgctc ctgactatgc 3420
caaagccaaa atatcagcag cccacatcat catgatcatt gaaaaaaccc ctttgattga 3480
cagctacagc acggaaggcc taatgccgaa cacattggaa ggaaatgtca catttggtga 3540
agttgtattc aactatccca cccgaccgga catcccagtg cttcagggac tgagcctgga 3600
ggtgaagaag ggccagacgc tggctctggt gggcagcagt ggctgtggga agagcacagt 3660
ggtccagctc ctggagcggt tctacgaccc cttggcaggg aaagtgctgc ttgatggcaa 3720
agaaataaag cgactgaatg ttcagtggct ccgagcacac ctgggcatcg tgtcccagga 3780
gcccatcctg tttgactgca gcattgctga gaacattgcc tatggagaca acagccgggt 3840
ggtgtcacag gaagagatcg tgagggcagc aaaggaggcc aacatacatg ccttcatcga 3900
gtcactgcct aataaatata gcactaaagt aggagacaaa ggaactcagc tctctggtgg 3960
ccagaaacaa cgcattgcca tagctcgtgc ccttgttaga cagcctcata ttttgctttt 4020
ggatgaagcc acgtcagctc tggatacaga aagtgaaaag gttgtccaag aagccctgga 4080
caaagccaga gaaggccgca cctgcattgt gattgctcac cgcctgtcca ccatccagaa 4140
tgcagactta atagtggtgt ttcagaatgg cagagtcaag gagcatggca cgcatcagca 4200
gctgctggca cagaaaggca tctatttttc aatggtcagt gtccaggctg gaacaattta 4260
gaagacccaa tttggggttt attacggcat ttgaaatttg agagttagaa gtgacacctg 4320
tcttgatgaa gtattgaaac aacaggctag ctctccctaa gttattagaa acatccagaa 4380
aaagaacaaa attcaaggta agtacaggtg tagaaatata gaagccacag acatagggaa 4440
atggtcttat ggtcctgaat gggttgggta gacaggaaag tttgggaata attttcccaa 4500
gtacaaaaga aaaataaatt gttcaatagc ctc 4533

<210> 31
<211> 2307
<212> DNA
<213> Homo sapiens

<400> 31
cctactctat tcagatattc tccagattcc taaagattag agatcatttc tcattctcct 60
aggagtactc acttcaggaa gcaaccagat aaaagagagg tgcaacggaa gccagaacat 120
tcctcctgga aattcaacct gtttcgcagt ttctcgagga atcagcattc agtcaatccg 180
ggccgggagc agtcatctgt ggtgaggctg attggctggg caggaacagc gccggggcgt 240
gggctgagca cagcgcttcg ctctctttgc cacaggaagc ctgagctcat tcgagtagcg 300
gctcttccaa gctcaaagaa gcagaggccg ctgttcgttt cctttaggtc tttccactaa 360
agtcggagta tcttcttcca agatttcacg tcttggtggc cgttccaagg agcgcgaggt 420
cgggatggat cttgaagggg accgcaatgg aggagcaaag aagaagaact tttttaaact 480
gaacaataaa agtgaaaaag ataagaagga aaagaaacca actgtcagtg tattttcaat 540
gtttcgctat tcaaattggc ttgacaagtt gtatatggtg gtgggaactt tggctgccat 600

catccatggg gctggacttc ctctcatgat gctggtgttt ggagaaatga cagatatctt 660
tgcaaatgca ggaaatttag aagatctgat gtcaaacatc actaatagaa gtgatatcaa 720
tgatacaggg ttcttcatga atctggagga agacatgacc aggtatgcct attattacag 780
tggaattggt gctggggtgc tggttgctgc ttacattcag gtttcatttt ggtgcctggc 840
agctggaaga caaatacaca aaattagaaa acagtttttt catgctataa tgcgacagga 900
gataggctgg tttgatgtgc acgatgttgg ggagcttaac acccgactta cagatgatgt 960
ctccaagatt aatgaaggaa ttggtgacaa aattggaatg ttctttcagt caatggcaac 1020
atttttcact gggtttatag taggatttac acgtggttgg aagctaaccc ttgtgatttt 1080
ggccatcagt cctgttcttg gactgtcagc tgctgtctgg gcaaagatac tatcttcatt 1140
tactgataaa gaactcttag cgtatgcaaa agctggagca gtagctgaag aggtcttggc 1200
agcaattaga actgtgattg catttggagg acaaaagaaa gaacttgaaa ggtacaacaa 1260
aaatttagaa gaagctaaaa gaattgggat aaagaaagct attacagcca atatttctat 1320
aggtgctgct ttcctgctga tctatgcatc ttatgctctg gccttctggt atgggaccac 1380
cttggtcctc tcaggggaat attctattgg acaagtactc actgtattyt tttctgtatt 1440
aattggggct tttagtgttg gacaggcatc tccaagcatt gaagcatttg caaatgcaag 1500
aggagcagct tatgaaatct tcaagataat tgataataag ccaagtattg acagctattc 1560
gaagagtggg cacaaaccag ataatattaa gggaaatttg gaattcagaa atgttcactt 1620
cagttaccca tctcgaaaag aagttaagat cttgaagggc ctgaacctga aggtgcagag 1680
tgggcagacg gtggccctgg ttggaaacag tggctgtggg aagagcacaa cagtccagct 1740
gatgcagagg ctctatgacc ccacagaggg gatggtcagt gttgatggac aggatattag 1800
gaccataaat gtaaggtttc tacgggaaat cattggtgtg gtgagtcagg aacctgtatt 1860
gtttgccacc acgatagctg aaaacattcg ctatggccgt gaaaatgtca ccatggatga 1920
gattgagaaa gctgtcaagg aagccaatgc ctatgacttt atcatgaaac tgcctcataa 1980
atttgacacc ctggttggag agagaggggc ccagctgagt ggtgggcaga agcagaggat 2040
cgccattgca cgtgccctgg ttcgcaaccc caagatcctt ctgctggatg aggccacgtc 2100
agcattggac acagaaagtg aagctgaggt acaggcagct ctggataagg tcagtagact 2160
ctaaaaagct gaaggaccac cacattgaaa cctattgaag attcttgcca gtgcttccgg 2220
agtctgggct gagaaacaga aacatagcaa atggagctac ctcatggagc tgtattgatt 2280
tctcctttct gtcaggttac attgtcc 2307

<210> 32
<211> 1712
<212> DNA
<213> Homo sapiens

<400> 32
gcttggattg cggagccgcg agcagcgctg ggtaacggcc gcggcgacca ccccggacgg 60
cccctgtccc cgctggcggg cttccctgtc gccgttcgct gcgctgccgg cttcttggtg 120
aatttttgga tgaagccatt aaattaattg cttgccatca tgagcagaag caagcgtgac 180
aacaattttt atagtgtaga gattggagat tctacattca cagtcctgaa acgatatcag 240
aatttaaaac ctataggctc aggagctcaa ggaatagtat gcgcagctta tgatgccatt 300
cttgaaagaa atgttgcaat caagaagcta agccgaccat ttcagaatca gactcatgcc 360
aagcgggcct acagagagct agttcttatg aaatgtgtta atcacaaaaa tataattggc 420
cttttgaatg ttttcacacc acagaaatcc ctagaagaat ttcaagatgt ttacatagtc 480
atggagctca tggatgcaaa tctttgccaa gtgattcaga tggagctaga tcatgaaaga 540
atgtcctacc ttctctatca gatgctgtgt ggaatcaagc accttcattc tgctggaatt 600
attcatcggg acttaaagcc cagtaatata gtagtaaaat ctgattgcac tttgaagatt 660
cttgacttcg gtctggccag gactgcagga acgagtttta tgatgacgcc ttatgtagtg 720
actcgctact acagagcacc cgaggtcatc cttggcatgg gctacaagga aaacggagga 780
agaatgggaa aaggcatatt cacaaggtta caataaggtg cctgtgagat ataaaattta 840
taactgccac atcctttctt aggaattttt aaatttctat tttcttgtaa tatgaataca 900
agaatacatt cttgtaaatg aatgtattga acattagtta tggagtattt ttcttagcta 960
cttgatatta gatattgatc agtggaataa agttattgaa cagcttggaa caccatgtcc 1020
tgaattcatg aagaaactgc aaccaacagt aaggacttac gttgaaaaca gacctaaata 1080
tgctggatat agctttgaga aactcttccc tgatgtcctt ttcccagctg actcagaaca 1140
caacaaactt aaagccagtc aggcaaggga tttgttatcc aaaatgctgg taatagatgc 1200
atctaaaagg atctctgtag atgaagctct ccaacacccg tacatcaatg tctggtatga 1260
tccttctgaa gcagaagctc caccaccaaa gatccctgac aagcagttag atgaaaggga 1320
acacacaata gaagagtgga aagaattgat atataaggaa gttatggact tggaggagag 1380
aaccaagaat ggagttatac gggggcagcc ctctccttta gcacaggtgc agcagtgatc 1440

aatggctctc agcatccatc atcatcgtcg tctgtcaatg atgtgtcttc aatgtcaaca 1500
gatccgactt tggcctctga tacagacagc agtctagaag cagcagctgg gcctctgggc 1560
tgctgtagat gactacttgg gccatcgggg ggtgggaggg atggggagtc ggttagtcat 1620
tgatagaact actttgaaaa caattcagtg gtcttatttt tgggtgattt ttcaaaaaat 1680
gtaggatttc attttgtagt aaagtagttt at 1712

<210> 33
<211> 1068
<212> DNA
<213> Homo sapiens

<400> 33
cattaattgc ttgccatcat gagcagaagc aagcgtgaca acaattttta tagtgtagag 60
attggagatt ctacattcac agtcctgaaa cgatatcaga atttaaaacc tataggctca 120
ggagctcaag gaatagtatg cgcagcttat gatgccattc ttgaaagaaa tgttgcaatc 180
aagaagctaa gccgaccatt tcagaatcag actcatgcca agcgggccta cagagagcta 240
gttcttatga aatgtgttaa tcacaaaaat ataattggcc ttttgaatgt tttcacacca 300
cagaaatccc tagaagaatt tcaagatgtt tacatagtca tggagctcat ggatgcaaat 360
ctttgccaag tgattcagat ggagctagat catgaaagaa tgtcctacct tctctatcag 420
atgctgtgtg gaatcaagca ccttcattct gctggaatta ttcatcggga cttaaagccc 480
agtaatatag tagtaaaatc tgattgcact ttgaagattc ttgacttcgg tctggccagg 540
actgcaggaa cgagttttat gatgacgcct tatgtagtga ctcgctacta cagagcaccc 600
gaggtcatcc ttggcatggg ctacaaggaa aacgtggatt tatggtctgt ggggtgcatt 660
atgggagaaa tggtttgcca caaaatcctc tttccaggaa gggactatat tgatcagtgg 720
aataaagtta ttgaacagct tggaacacca tgtcctgaat tcatgaagaa actgcaacca 780
acagtaagga cttacgttga aaacagacct aaatatgctg gatatagctt tgagaaactc 840
ttccctgatg tccttttccc agctgactca gaacacaaca aacttaaagc cagtcagtac 900
tttttacaaa tatgtacatt taatcccatt tggggtgtgt agtgtgtgtg tnatgggttt 960
ggtgtttata tgtattcata ttcttatggg acatgaaccc aaggttttct ctggatggtg 1020
gggaaaaaaa tgaggttttt gttttttttt tctttaatct tatatatt 1068

<210> 34
<211> 1388
<212> DNA
<213> Homo sapiens

<400> 34
cattaattgc ttgccatcat gagcagaagc aagcgtgaca acaattttta tagtgtagag 60
attggagatt ctacattcac agtcctgaaa cgatatcaga atttaaaacc tataggctca 120
ggagctcaag gaatagtatg cgcagcttat gatgccattc ttgaaagaaa tgttgcaatc 180
aagaagctaa gccgaccatt tcagaatcag actcatgcca agcgggccta cagagagcta 240
gttcttatga aatgtgttaa tcacaaaaat ataattggcc ttttgaatgt tttcacacca 300
cagaaatccc tagaagaatt tcaagatgtt tacatagtca tggagctcat ggatgcaaat 360
ctttgccaag tgattcagat ggagctagat catgaaagaa tgtcctacct tctctatcag 420
atgctgtgtg gaatcaagca ccttcattct gctggaatta ttcatcggga cttaaagccc 480
agtaatatag tagtaaaatc tgattgcact ttgaagattc ttgacttcgg tctggccagg 540
actgcaggaa cgagttttat gatgacgcct tatgtagtga ctcgctacta cagagcaccc 600
gaggtcatcc ttggcatggg ctacaaggaa aacgtggatt tatggtctgt ggggtgcatt 660
atgggagaaa tggtttgcca caaaatcctc tttccaggaa gggactatat tgatcagtgg 720
aataaagtta ttgaacagct tggaacacca tgtcctgaat tcatgaagaa actgcaacca 780
acagtaagga cttacgttga aaacagacct aaatatgctg gatatagctt tgagaaactc 840
ttccctgatg tccttttccc agctgactca gaacacaaca aacttaaagc cagtcaggca 900
agggatttgt tatccaaaat gctggtaata gatgcatcta aaaggatctc tgtagatgaa 960
gctctccaac acccgtacat caatgtctgg tatgatcctt ctgaagcaga agctagaagc 1020
tgtaagttat tttcttaatg tttacagaac atattgcatt cttagagtta gaatgacagt 1080
taggtttgga ggagaccttt taattttaaa taaaaatgta gatacatgat gatgatgttt 1140
ttctgtttct tcatgaagac tacgtcaaat aaactaatga acatattcga gcccctccta 1200
cacaaaataa agttacctcc cactgttttt tgcaatcttg cctggatacc taaccagaga 1260
actaggatgt tgaatgctct gggggaacat cctaactcag gtataaaaca aattactgta 1320

tccaaaggaa aacagaattc tgtgatctgt gatataaata aaatgtggca atttcaagag 1380
ctagaaga 1388

<210> 35
<211> 1452
<212> DNA
<213> Homo sapiens

<400> 35
gcccgcagtg gcttttaccg ccaggaggtg accaagacgg cctgggaggt gcgcgccgtg 60
taccgggacc tgcagcccgt gggctcgggc gcctacggcg cggtgtgctc ggccgtggac 120
ggccgcaccg gcgctaaggt ggccatcaag aagctgtatc ggcccttcca gtccgagctg 180
ttcgccaagc gcgcctaccg cgagctgcgc ctgctcaagc acatgcgcca cgagaacgtg 240
atcgggctgc tggacgtatt cactcctgat gagaccctgg atgacttcac ggacttttac 300
ctggtgatgc cgttcatggg caccgacctg ggcaagctca tgaaacatga gaagctaggc 360
gaggaccgga tccagttcct cgtgtaccag atgctgaagg ggctgaggta tatccacgct 420
gccggcatca tccacagagt gagtcccggt ggagaagccg ctcatcagcc ctcccccagt 480
gcaatccccc cgcctccacg tcccacctgt gaggatgtga tggggtctgg gtgctgagcc 540
acgccctatg cacagcccct ggtgggaacc tgcctgggtg cccaggacct gaagcccggc 600
aacctggctg tgaacgaaga ctgtgagctg aagatcctgg acttcggcct ggccaggcag 660
gcagacagtg agatgactgg gtacgtggtg acccggtggt accgggctcc cgaggtcatc 720
ttgaattgga tgcgctacac gcagacggtg gacatctggt ctgtgggctg catcatggcg 780
gagatgatca caggcaagac gctgttcaag ggcagcgacc acctggacca gctgaaggag 840
atcatgaagg tgacngggga cgcctccggc tgagtttgtg cagcggctgc agagcgatga 900
ggccaagaac tacatgaagg gcctccccga attggagaag aaggattttg cctctatcct 960
gaccaatgca agccctctgg ctgtgaacct cctggagaag atgctggtgc tggacgcgga 1020
gcagcgggtg acggcaggcg aggcgctggc ccatccctac ttcgagtccc tgcacgacac 1080
ggaagatgag ccccaggtcc agaagtatga tgactccttt gacgacgttg accgcacact 1140
ggatgaatgg aagcgtgtta cttacaaaga ggtgctcagc ttcaagcctn cccggcaggc 1200
tgggggccag ggtctncaan gagacgcctn tgtgaagatc tcttgggctt ccggggtggg 1260
cagtgaggac caccttcacc ttccacctga gaggggactc tcgntggcac cttgaccttg 1320
gctggggctt gcattccaag gcatccattc agacagacgc ccgggttcct ggaccctnct 1380
tcccacgggc atgcctntgt cttgggcgcc catatggang agcnctgact ttctggacaa 1440
anctctggnc ca 1452

<210> 36
<211> 2355
<212> DNA
<213> Homo sapiens

<400> 36
gaattccgcc agccccgcca gtccccgcgc agtccccgcg cagtcccagc gccaccgggc 60
agcagcggcg ccgtgctcgc tccagggcgc aaccatgtcg ccatttcttc ggattggctt 120
gtccaacttt gactgcgggt cctgccagtc ttgtcagggc gaggctgtta acccttactg 180
tgctgtgctc gtcaaagagt atgtcgaatc agagaacggg cagatgtata tccagaaaaa 240
gcctaccatg tacccaccct gggacagcac ttttgatgcc catatcaaca agggaagagt 300
catgcagatc attgtgaaag gcaaaaacgt ggacctcatc tctgaaacca ccgtggagct 360
ctactcgctg gctgagaggt gcaggaagaa caacgggaag acagaaatat ggttagagct 420
gaaacctcaa ggccgaatgc taatgaatgc aagatacttt ctggaaatga gtgacacaaa 480
ggacatgaat gaatttgaga cggaaggctt ctttgctttg catcagcgcc ggggtgccat 540
caagcaggca aaggtccacc acgtcaagtg ccacgagttc actgccacct tcttcccaca 600
gcccacattt tgctctgtct gccacgagtt tgtctggggc ctgaacaaac agggctacca 660
gtgccgacaa tgcaatgcag caattcacaa gaagtgtatt gataaagtta tagcaaagtg 720
cacaggatca gctatcaata gccgagaaac catgttccac aaggagagat tcaaaattga 780
catgccacac agatttaaag tctacaatta caagagcccg accttctgtg aacactgtgg 840
gaccctgctg tggggactgg cacggcaagg actcaagtgt gatgcatgtg gcatgaatgt 900
gcatcataga tgccagacaa aggtggccaa cctttgtggc ataaaccaga agctaatggc 960
tgaagcgctg gccatgattg agagcactca acaggctcgc tgcttaagag atactgaaca 1020
gatcttcaga gaaggtccgg ttgaaattgg tctcccatgc tccatcaaaa atgaagcaag 1080

```
gccgccatgt ttaccgacac cgggaaaaag agagcctcag ggcatttcct gggagtctcc 1140
gttggatgag gtggataaaa tgtgccatct tccagaacct gaactgaaca aagaaagacc 1200
atctctgcag attaaactaa aaattgagga ttttatcttg cacaaaatgt tggggaaagg 1260
aagttttggc aaggtcttcc tggcagaatt caagaaaacc aatcaatttt tcgcaataaa 1320
ggccttaaag aaagatgtgg tcttgatgga cgatgatgtt gagtgcacga tggtagagaa 1380
gagagttctt tccttggcct gggagcatcc gtttctgacg cacatgtttt gtacattcca 1440
gaccaaggaa aacctctttt ttgtgatgga gtacctcaac ggaggggact taatgtacca 1500
catccaaagc tgccacaagt tcgacctttc cagagcgacg ttttatgctg ctgaaatcat 1560
tcttggtctg cagttccttc attccaaagg aatagtctac agggacctga agctagataa 1620
catcctgtta gacaaagatg gacatatcaa gatcgcggat tttggaatgt gcaaggagaa 1680
catgttagga gatgccaaga cgaatacctt ctgtgggaca cctgactaca tcgccccaga 1740
gatcttgctg ggtcagaaat acaaccactc tgtggactgg tggtccttcg gggttctcct 1800
ttatgaaatg ctgattggtc agtcgccttt ccacgggcag gatgaggagg agctcttcca 1860
ctccatccgc atggacaatc ccttttaccc acggtggctg gagaaggaag caaaggacct 1920
tctggtgaag gtaagaagcg aagccaagag cgtcttcata agacgagcat taggtcttct 1980
ggtcagtttt ctgttcctct tagtttccaa cttgcatgtg gcaaacaatg attattattg 2040
aactgggttt aaatgggatg tgcaccgtct gtgttttaat agaggcacca atattatgag 2100
cattaaatgt caaaatgagt gtaagagaaa ccctcatgtg catcagttat aacataacgg 2160
ccccaggaac cagttccatg gaccttgaat acgctcacct ggagatgtag ttggttcatt 2220
aaacaagcac agtgtgtggc ttaaaaatca atcttctagc tacttgggag gttgaggcag 2280
gaggattgaa gttggaagtg tgaggtcagc ctgggcaatg tatcgagacc cctgtctcca 2340
aaacaataaa gggga                                                  2355
```

<210> 37
<211> 497
<212> PRT
<213> Homo sapiens

<400> 37

```
Met Val Arg Ser Gly Asn Lys Ala Ala Val Val Leu Cys Met Asp Val
  1               5                  10                  15

Gly Phe Thr Met Ser Asn Ser Ile Pro Gly Ile Glu Ser Pro Phe Glu
             20                  25                  30

Gln Ala Lys Lys Val Ile Thr Met Phe Val Gln Arg Gln Val Phe Ala
         35                  40                  45

Glu Asn Lys Asp Glu Ile Ala Leu Val Leu Phe Gly Thr Asp Gly Thr
     50                  55                  60

Asp Asn Pro Leu Ser Gly Gly Asp Gln Tyr Gln Asn Ile Thr Val His
 65                  70                  75                  80

Arg His Leu Met Leu Pro Asp Phe Asp Leu Leu Glu Asp Ile Glu Ser
                 85                  90                  95

Lys Ile Gln Pro Gly Ser Gln Gln Ala Asp Phe Leu Asp Ala Leu Ile
            100                 105                 110

Val Ser Met Asp Val Ile Gln His Glu Thr Ile Gly Lys Lys Phe Glu
        115                 120                 125

Lys Arg His Ile Glu Ile Phe Thr Asp Leu Ser Ser Arg Phe Ser Lys
    130                 135                 140

Ser Gln Leu Asp Ile Ile Ile His Ser Leu Lys Lys Cys Asp Ile Ser
145                 150                 155                 160

Leu Gln Phe Phe Leu Pro Phe Ser Leu Gly Lys Glu Asp Gly Ser Gly
```

```
                 165                 170                 175

Asp Arg Gly Asp Gly Pro Phe Arg Leu Gly Gly His Gly Pro Ser Phe
            180                 185                 190

Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu Gly Leu Glu Ile Val
        195                 200                 205

Lys Met Val Met Ile Ser Leu Glu Gly Glu Asp Gly Leu Asp Glu Ile
    210                 215                 220

Tyr Ser Phe Ser Glu Ser Leu Arg Lys Leu Cys Val Phe Lys Lys Ile
225                 230                 235                 240

Glu Arg His Ser Ile His Trp Pro Cys Arg Leu Thr Ile Gly Ser Asn
                245                 250                 255

Leu Ser Ile Arg Ile Ala Ala Tyr Lys Ser Ile Leu Gln Glu Arg Val
            260                 265                 270

Lys Lys Thr Trp Thr Val Val Asp Ala Lys Thr Leu Lys Lys Glu Asp
        275                 280                 285

Ile Gln Lys Glu Thr Val Tyr Cys Leu Asn Asp Asp Asp Glu Thr Glu
    290                 295                 300

Val Leu Lys Glu Asp Ile Ile Gln Gly Phe Arg Tyr Gly Ser Asp Ile
305                 310                 315                 320

Val Pro Phe Ser Lys Val Asp Glu Glu Gln Met Lys Tyr Lys Ser Glu
                325                 330                 335

Gly Lys Cys Phe Ser Val Leu Gly Phe Cys Lys Ser Ser Gln Val Gln
            340                 345                 350

Arg Arg Phe Phe Met Gly Asn Gln Val Leu Lys Val Phe Ala Ala Arg
        355                 360                 365

Asp Asp Glu Ala Ala Ala Val Ala Leu Ser Ser Leu Ile His Ala Leu
    370                 375                 380

Asp Asp Leu Asp Met Val Ala Ile Val Arg Tyr Ala Tyr Asp Lys Arg
385                 390                 395                 400

Ala Asn Pro Gln Val Gly Val Ala Phe Pro His Ile Lys His Asn Tyr
                405                 410                 415

Glu Cys Leu Val Tyr Val Gln Leu Pro Phe Met Glu Asp Leu Arg Gln
            420                 425                 430

Tyr Met Phe Ser Ser Leu Lys Asn Ser Lys Lys Tyr Ala Pro Thr Glu
        435                 440                 445

Ala Gln Leu Asn Ala Val Asp Ala Leu Ile Asp Ser Met Ser Leu Ala
    450                 455                 460

Lys Lys Asp Glu Lys Thr Asp Thr Leu Glu Asp Leu Phe Pro Thr Thr
465                 470                 475                 480

Lys Ile Pro Asn Pro Arg Phe Gln Arg Leu Phe Gln Val Arg Glu Glu
                485                 490                 495
```

Gly

<210> 38
<211> 521
<212> PRT
<213> Homo sapiens

<400> 38

```
Met Val Arg Ser Gly Asn Lys Ala Ala Val Val Leu Cys Met Asp Val
  1               5                  10                  15

Gly Phe Thr Met Ser Asn Ser Ile Pro Gly Ile Glu Ser Pro Phe Glu
             20                  25                  30

Gln Ala Lys Lys Val Ile Thr Met Phe Val Gln Arg Gln Val Phe Ala
         35                  40                  45

Glu Asn Lys Asp Glu Ile Ala Leu Val Leu Phe Gly Thr Asp Gly Thr
     50                  55                  60

Asp Asn Pro Leu Ser Gly Gly Asp Gln Tyr Gln Asn Ile Thr Val His
 65                  70                  75                  80

Arg His Leu Met Leu Pro Asp Phe Asp Leu Leu Glu Asp Ile Glu Ser
                 85                  90                  95

Lys Ile Gln Pro Gly Ser Gln Gln Ala Asp Phe Leu Asp Ala Leu Ile
            100                 105                 110

Val Ser Met Asp Val Ile Gln His Glu Thr Ile Gly Lys Lys Phe Glu
        115                 120                 125

Lys Arg His Ile Glu Ile Phe Thr Asp Leu Ser Ser Arg Phe Ser Lys
    130                 135                 140

Ser Gln Leu Asp Ile Ile Ile His Ser Leu Lys Lys Cys Asp Ile Ser
145                 150                 155                 160

Leu Gln Phe Phe Leu Pro Phe Ser Leu Gly Lys Glu Asp Gly Ser Gly
                165                 170                 175

Asp Arg Gly Asp Gly Pro Phe Arg Leu Gly Gly His Gly Pro Ser Phe
            180                 185                 190

Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu Gly Leu Glu Ile Val
        195                 200                 205

Lys Met Val Met Ile Ser Leu Glu Gly Glu Asp Gly Leu Asp Glu Ile
    210                 215                 220

Tyr Ser Phe Ser Glu Ser Leu Arg Lys Leu Cys Val Phe Lys Lys Ile
225                 230                 235                 240

Glu Arg His Ser Ile His Trp Pro Cys Arg Leu Thr Ile Gly Ser Asn
                245                 250                 255

Leu Ser Ile Arg Ile Ala Ala Tyr Lys Ser Ile Leu Gln Glu Arg Val
```

```
            260                 265                 270

Lys Lys Thr Trp Thr Val Val Asp Ala Lys Thr Leu Lys Lys Glu Asp
        275                 280                 285

Ile Gln Lys Glu Thr Val Tyr Cys Leu Asn Asp Asp Asp Glu Thr Glu
    290                 295                 300

Leu Asn Pro Pro Ala Glu Val Thr Thr Lys Ser Gln Ile Pro Leu Ser
305                 310                 315                 320

Lys Ile Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Gln
                325                 330                 335

Val Thr Ala Gln Glu Ile Phe Gln Asp Asn His Glu Asp Gly Pro Thr
            340                 345                 350

Ala Lys Lys Leu Lys Thr Glu Gln Gly Gly Ala His Phe Ser Val Ser
        355                 360                 365

Ser Leu Ala Glu Gly Ser Val Thr Ser Val Gly Ser Val Asn Pro Ala
    370                 375                 380

Glu Asn Phe Arg Val Leu Val Lys Gln Lys Lys Ala Ser Phe Glu Glu
385                 390                 395                 400

Ala Ser Asn Gln Leu Ile Asn His Ile Glu Gln Phe Leu Asp Thr Asn
                405                 410                 415

Glu Thr Pro Tyr Phe Met Lys Ser Ile Asp Cys Ile Arg Ala Phe Arg
            420                 425                 430

Glu Glu Ala Ile Lys Phe Ser Glu Glu Gln Arg Phe Asn Asn Phe Leu
        435                 440                 445

Lys Ala Leu Gln Glu Lys Val Glu Ile Lys Gln Leu Asn His Phe Trp
    450                 455                 460

Glu Ile Val Val Gln Asp Gly Ile Thr Leu Ile Thr Lys Glu Glu Ala
465                 470                 475                 480

Ser Gly Ser Ser Val Thr Ala Glu Glu Ala Lys Lys Phe Leu Ala Pro
                485                 490                 495

Lys Asp Lys Pro Ser Gly Asp Thr Ala Ala Val Phe Glu Glu Gly Gly
            500                 505                 510

Asp Val Asp Asp Leu Leu Asp Met Ile
        515                 520
```

<210> 39
<211> 437
<212> PRT
<213> Homo sapiens

<400> 39

```
Met Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn
  1               5                  10                  15
```

```
Ile Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly
            20                  25                  30

Lys Gly Thr Leu Leu Ile Arg Asn Gly Ser Glu Val Arg Asp Pro Leu
        35                  40                  45

Val Thr Tyr Glu Gly Ser Asn Pro Pro Ala Ser Pro Leu Gln Asp Asn
    50                  55                  60

Leu Val Ile Ala Leu His Ser Tyr Glu Pro Ser His Asp Gly Asp Leu
65                  70                  75                  80

Gly Phe Glu Lys Gly Glu Gln Leu Arg Ile Leu Glu Gln Ser Gly Glu
                85                  90                  95

Trp Trp Lys Ala Gln Ser Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro
            100                 105                 110

Phe Asn Phe Val Ala Lys Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe
        115                 120                 125

Phe Lys Asn Leu Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro
    130                 135                 140

Gly Asn Thr His Gly Ser Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala
145                 150                 155                 160

Gly Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Gln Asn Gln Gly Glu
                165                 170                 175

Val Val Lys His Tyr Lys Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr
            180                 185                 190

Ile Ser Pro Arg Ile Thr Phe Pro Gly Leu His Glu Leu Val Arg His
        195                 200                 205

Tyr Thr Asn Ala Ser Asp Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys
    210                 215                 220

Gln Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val
225                 230                 235                 240

Pro Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe
                245                 250                 255

Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val
            260                 265                 270

Lys Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu
        275                 280                 285

Ala Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr
    290                 295                 300

Ala Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu
305                 310                 315                 320

Asn Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu
                325                 330                 335

Thr Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met
```

```
            340                 345                 350

Ala Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala
        355                 360                 365

Asn Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly
    370                 375                 380

Leu Ala Arg Leu Ile Glu Asp Ile His His Gln Val Arg Cys Val Val
385                 390                 395                 400

Phe Trp Asp Pro Ala Asp Gly Asn Cys His Pro Arg Pro His Pro Leu
                405                 410                 415

Pro Arg Asp Asp Gln Pro Gly Gly Asp Ser Glu Pro Gly Ala Arg Leu
            420                 425                 430

Pro His Gly Ala Pro
        435
```

<210> 40
<211> 567
<212> PRT
<213> Homo sapiens

<400> 40

```
Met Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn
  1               5                  10                  15

Ile Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly
            20                  25                  30

Lys Gly Thr Leu Leu Ile Arg Asn Gly Ser Glu Val Arg Asp Pro Leu
        35                  40                  45

Val Thr Tyr Glu Gly Ser Asn Pro Pro Ala Ser Pro Leu Gln Gly Asp
    50                  55                  60

Pro Arg Gln Gln Gly Leu Lys Asp Lys Ala Cys Gly Ser Leu Ala Val
65                  70                  75                  80

Gly Phe His Leu Ser Pro Thr Tyr Phe Leu Pro Gly Leu Ala Phe Leu
                85                  90                  95

Val Pro His Pro Val Thr Pro Gly Phe Leu Pro Ile Pro Ala Arg Phe
            100                 105                 110

Ser Leu Thr Pro Leu Val Phe Thr Asp Asn Leu Val Ile Ala Leu His
        115                 120                 125

Ser Tyr Glu Pro Ser His Asp Gly Asp Leu Gly Phe Glu Lys Gly Glu
    130                 135                 140

Gln Leu Arg Ile Leu Glu Gln Ser Gly Glu Trp Trp Lys Ala Gln Ser
145                 150                 155                 160

Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro Phe Asn Phe Val Ala Lys
                165                 170                 175
```

Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe Phe Lys Asn Leu Ser Arg
180 185 190

Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro Gly Asn Thr His Gly Ser
195 200 205

Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala Gly Ser Phe Ser Leu Ser
210 215 220

Val Arg Asp Phe Asp Gln Asn Gln Gly Glu Val Val Lys His Tyr Lys
225 230 235 240

Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr Ile Ser Pro Arg Ile Thr
245 250 255

Phe Pro Gly Leu His Glu Leu Val Arg His Tyr Thr Asn Ala Ser Asp
260 265 270

Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys Gln Thr Gln Lys Pro Gln
275 280 285

Lys Pro Trp Trp Glu Asp Glu Trp Glu Val Pro Arg Glu Thr Leu Lys
290 295 300

Leu Val Glu Arg Leu Gly Ala Gly Gln Phe Gly Glu Val Trp Met Gly
305 310 315 320

Tyr Tyr Asn Gly His Thr Lys Val Ala Val Lys Ser Leu Lys Gln Gly
325 330 335

Ser Met Ser Pro Asp Ala Phe Leu Ala Glu Ala Asn Leu Met Lys Gln
340 345 350

Leu Gln His Gln Arg Leu Val Arg Leu Tyr Ala Val Val Thr Gln Glu
355 360 365

Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Val Asp
370 375 380

Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu Thr Ile Asn Lys Leu Leu
385 390 395 400

Asp Met Ala Ala Gln Ile Ala Glu Gly Met Ala Phe Ile Glu Glu Arg
405 410 415

Asn Tyr Ile His Arg Asp Leu Arg Ala Ala Asn Ile Leu Val Ser Asp
420 425 430

Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly Leu Ala Arg Leu Ile Glu
435 440 445

Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile Lys Trp
450 455 460

Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr Phe Thr Ile Lys Ser Asp
465 470 475 480

Val Trp Ser Phe Gly Ile Leu Leu Thr Glu Ile Val Thr His Gly Arg
485 490 495

Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu Val Ile Gln Asn Leu Glu

```
            500                 505                 510

Arg Gly Tyr Arg Met Val Arg Pro Asp Asn Cys Pro Glu Glu Leu Tyr
        515                 520                 525

Gln Leu Met Arg Leu Cys Trp Lys Glu Arg Pro Glu Asp Arg Pro Thr
    530                 535                 540

Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp Phe Phe Thr Ala Thr Glu
545                 550                 555                 560

Gly Gln Tyr Gln Pro Gln Pro
                565
```

<210> 41
<211> 192
<212> PRT
<213> Homo sapiens

<400> 41

```
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
  1               5                  10                  15

Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
             20                  25                  30

Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
         35                  40                  45

Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Asn Ala Val Ser Ser Glu
     50                  55                  60

Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro Ser Lys Ser Asn Glu
65                  70                  75                  80

Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp Asp His
                85                  90                  95

Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp
            100                 105                 110

Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu
        115                 120                 125

Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu
    130                 135                 140

Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly
145                 150                 155                 160

Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg
                165                 170                 175

Pro Asp Ile Gln Val Asn Pro Leu Thr Asp Thr Pro Asp Gly Ser Asp
            180                 185                 190
```

<210> 42
<211> 109
<212> PRT
<213> Homo sapiens

<400> 42
Met Glu Leu Gly Leu Pro Gln Val Pro Pro Ala Val Asp Ala Glu Leu
1 5 10 15

Leu Cys Arg Phe Val Asp Arg Gly Leu Pro Tyr Pro Asp Val Ser Ser
20 25 30

Ala Asn Thr Pro Pro Ala Val Gly Leu Ser Pro Pro Thr Pro Tyr Phe
35 40 45

Glu Pro Cys Ala Leu Pro Ser Pro His Arg His Gln Leu Ala Glu Ala
50 55 60

Ile Pro Cys Thr Leu Ala Val Ser Asn Pro His Thr Asp Ala Trp Lys
65 70 75 80

Ser His Gly Leu Val Glu Val Ala Ser Tyr Cys Glu Glu Ser Arg Gly
85 90 95

Asn Asn Gln Trp Val Pro Tyr Ile Ser Leu Gln Glu Arg
100 105

<210> 43
<211> 331
<212> PRT
<213> Homo sapiens

<400> 43
Met Arg Ala Arg Pro Gln Val Cys Glu Ala Leu Leu Phe Ala Leu Ala
1 5 10 15

Leu Gln Thr Gly Val Cys Tyr Gly Ile Lys Trp Leu Ala Leu Ser Lys
20 25 30

Thr Pro Ser Ala Leu Ala Leu Asn Gln Thr Gln His Cys Lys Gln Leu
35 40 45

Glu Gly Leu Val Ser Ala Gln Val Gln Leu Cys Arg Ser Asn Leu Glu
50 55 60

Leu Met His Thr Val Val His Ala Ala Arg Glu Val Met Lys Ala Cys
65 70 75 80

Arg Arg Ala Phe Ala Asp Met Arg Trp Asn Cys Ser Ser Ile Glu Leu
85 90 95

Ala Pro Asn Tyr Leu Leu Asp Leu Glu Arg Gly Thr Arg Glu Ser Ala
100 105 110

Phe Val Tyr Ala Leu Ser Ala Ala Ala Ile Ser His Ala Ile Ala Arg
115 120 125

```
Ala Cys Thr Ser Gly Asp Leu Pro Gly Cys Ser Cys Gly Pro Val Pro
    130                 135                 140

Gly Glu Pro Pro Gly Pro Gly Asn Arg Trp Gly Arg Cys Ala Asp Asn
145                 150                 155                 160

Leu Ser Tyr Gly Leu Leu Met Gly Ala Lys Phe Ser Asp Ala Pro Met
            165                 170                 175

Lys Val Lys Lys Thr Gly Ser Gln Ala Asn Lys Leu Met Arg Leu His
        180                 185                 190

Asn Ser Glu Val Gly Arg Gln Ala Leu Arg Ala Ser Leu Glu Met Lys
    195                 200                 205

Cys Lys Cys His Gly Val Ser Gly Ser Cys Ser Ile Arg Thr Cys Trp
    210                 215                 220

Lys Gly Leu Gln Glu Leu Gln Asp Val Ala Ala Asp Leu Lys Thr Arg
225                 230                 235                 240

Tyr Leu Ser Ala Thr Lys Val Val His Arg Pro Met Gly Thr Arg Lys
            245                 250                 255

His Leu Val Pro Lys Asp Leu Asp Ile Arg Pro Val Lys Asp Ser Glu
        260                 265                 270

Leu Val Tyr Leu Gln Ser Ser Pro Asp Phe Cys Met Lys Asn Glu Lys
    275                 280                 285

Val Gly Ser His Gly Thr Gln Asp Arg Gln Cys Asn Lys Thr Ser Asn
    290                 295                 300

Gly Ser Asp Ser Cys Asp Leu Met Cys Cys Tyr Val Thr Cys Arg Arg
305                 310                 315                 320

Cys Glu Arg Thr Val Glu Arg Tyr Val Cys Lys
            325                 330
```

<210> 44
<211> 237
<212> PRT
<213> Homo sapiens

<400> 44

```
Met Arg Ala Arg Pro Gln Val Cys Glu Ala Leu Leu Phe Ala Leu Ala
  1               5                  10                  15

Leu Gln Thr Gly Val Cys Tyr Gly Ile Lys Trp Leu Ala Leu Ser Lys
            20                  25                  30

Thr Pro Ser Ala Leu Ala Leu Asn Gln Thr Gln His Cys Lys Gln Leu
        35                  40                  45

Glu Gly Leu Val Ser Ala Gln Val Gln Leu Cys Arg Ser Asn Leu Glu
    50                  55                  60

Leu Met His Thr Val Val His Ala Ala Arg Glu Val Met Lys Ala Cys
65                  70                  75                  80
```

```
Arg Arg Ala Phe Ala Asp Met Arg Trp Asn Cys Ser Ser Ile Glu Leu
                 85                  90                  95

Ala Pro Asn Tyr Leu Leu Asp Leu Glu Arg Gly Thr Arg Glu Ser Ala
            100                 105                 110

Phe Val Tyr Ala Ala Ala Asp Leu Lys Thr Arg Tyr Leu Ser Ala Thr
        115                 120                 125

Lys Val Val His Arg Pro Met Gly Thr Arg Lys His Leu Val Pro Lys
    130                 135                 140

Asp Leu Asp Ile Arg Pro Val Lys Asp Ser Glu Leu Val Tyr Leu Gln
145                 150                 155                 160

Ser Ser Pro Asp Phe Cys Met Lys Asn Glu Lys Val Gly Ser His Gly
                165                 170                 175

Thr Gln Asp Arg Gln Cys Asn Lys Thr Ser Asn Gly Ser Asp Ser Cys
            180                 185                 190

Asp Leu Met Cys Cys Gly Arg Gly Tyr Asn Pro Tyr Thr Asp Arg Val
        195                 200                 205

Val Glu Arg Cys His Cys Lys Tyr His Trp Cys Cys Tyr Val Thr Cys
    210                 215                 220

Arg Arg Cys Glu Arg Thr Val Glu Arg Tyr Val Cys Lys
225                 230                 235
```

<210> 45
<211> 615
<212> PRT
<213> Homo sapiens

<400> 45

```
Met Ser Pro Phe Leu Arg Ile Gly Leu Ser Asn Phe Asp Cys Gly Ser
  1               5                  10                  15

Cys Gln Ser Cys Gln Gly Glu Ala Val Asn Pro Tyr Cys Ala Val Leu
             20                  25                  30

Val Lys Glu Tyr Val Glu Ser Glu Asn Gly Gln Met Tyr Ile Gln Lys
         35                  40                  45

Lys Pro Thr Met Tyr Pro Pro Trp Asp Ser Thr Phe Asp Ala His Ile
     50                  55                  60

Asn Lys Gly Arg Val Met Gln Ile Ile Val Lys Gly Lys Asn Val Asp
 65                  70                  75                  80

Leu Ile Ser Glu Thr Thr Val Glu Leu Tyr Ser Leu Ala Glu Arg Cys
                85                  90                  95

Arg Lys Asn Asn Gly Lys Thr Glu Ile Trp Leu Glu Leu Lys Pro Gln
            100                 105                 110

Gly Arg Met Leu Met Asn Ala Arg Tyr Phe Leu Glu Met Ser Asp Thr
```

```
        115                 120                 125

Lys Asp Met Asn Glu Phe Glu Thr Glu Gly Phe Phe Ala Leu His Gln
    130                 135                 140

Arg Arg Gly Ala Ile Lys Gln Ala Lys Val His His Val Lys Cys His
145                 150                 155                 160

Glu Phe Thr Ala Thr Phe Phe Pro Gln Pro Thr Phe Cys Ser Val Cys
                165                 170                 175

His Glu Phe Val Trp Gly Leu Asn Lys Gln Gly Tyr Gln Cys Arg Gln
            180                 185                 190

Cys Asn Ala Ala Ile His Lys Lys Cys Ile Asp Lys Val Ile Ala Lys
        195                 200                 205

Cys Thr Gly Ser Ala Ile Asn Ser Arg Glu Thr Met Phe His Lys Glu
    210                 215                 220

Arg Phe Lys Ile Asp Met Pro His Arg Phe Lys Val Tyr Asn Tyr Lys
225                 230                 235                 240

Ser Pro Thr Phe Cys Glu His Cys Gly Thr Leu Leu Trp Gly Leu Ala
                245                 250                 255

Arg Gln Gly Leu Lys Cys Asp Ala Cys Gly Met Asn Val His His Arg
            260                 265                 270

Cys Gln Thr Lys Val Ala Asn Leu Cys Gly Ile Asn Gln Lys Leu Met
        275                 280                 285

Ala Glu Ala Leu Ala Met Ile Glu Ser Thr Gln Gln Ala Arg Cys Leu
    290                 295                 300

Arg Asp Thr Glu Gln Ile Phe Arg Glu Gly Pro Val Glu Ile Gly Leu
305                 310                 315                 320

Pro Cys Ser Ile Lys Asn Glu Ala Arg Pro Pro Cys Leu Pro Thr Pro
                325                 330                 335

Gly Lys Arg Glu Pro Gln Gly Ile Ser Trp Glu Ser Pro Leu Asp Glu
            340                 345                 350

Val Asp Lys Met Cys His Leu Pro Glu Pro Glu Leu Asn Lys Glu Arg
        355                 360                 365

Pro Ser Leu Gln Ile Lys Leu Lys Ile Glu Asp Phe Ile Leu His Lys
    370                 375                 380

Met Leu Gly Lys Gly Ser Phe Gly Lys Val Phe Leu Ala Glu Phe Lys
385                 390                 395                 400

Lys Thr Asn Gln Phe Phe Ala Ile Lys Ala Leu Lys Lys Asp Val Val
                405                 410                 415

Leu Met Asp Asp Asp Val Glu Cys Thr Met Val Glu Lys Arg Val Leu
            420                 425                 430

Ser Leu Ala Trp Glu His Pro Phe Leu Thr His Met Phe Cys Thr Phe
        435                 440                 445
```

```
Gln Thr Lys Glu Asn Leu Phe Phe Val Met Glu Tyr Leu Asn Gly Gly
    450                 455                 460

Asp Leu Met Tyr His Ile Gln Ser Cys His Lys Phe Asp Leu Ser Arg
465                 470                 475                 480

Ala Thr Phe Tyr Ala Ala Glu Ile Ile Leu Gly Leu Gln Phe Leu His
                485                 490                 495

Ser Lys Gly Ile Val Tyr Arg Asp Leu Lys Leu Asp Asn Ile Leu Leu
            500                 505                 510

Asp Lys Asp Gly His Ile Lys Ile Ala Asp Phe Gly Met Cys Lys Glu
        515                 520                 525

Asn Met Leu Gly Asp Ala Lys Thr Asn Thr Phe Cys Gly Thr Pro Asp
    530                 535                 540

Tyr Ile Ala Pro Glu Ile Leu Leu Gly Gln Lys Tyr Asn His Ser Val
545                 550                 555                 560

Asp Trp Trp Ser Phe Gly Val Leu Leu Tyr Glu Met Leu Ile Gly Gln
                565                 570                 575

Ser Pro Phe His Gly Gln Asp Glu Glu Glu Leu Phe His Ser Ile Arg
            580                 585                 590

Met Asp Asn Pro Phe Tyr Pro Arg Trp Leu Glu Lys Glu Ala Lys Asp
        595                 600                 605

Leu Leu Val Lys Val Arg Ser
    610                 615
```

<210> 46
<211> 292
<212> PRT
<213> Homo sapiens

<400> 46

```
Met Pro Ile Thr Arg Met Arg Met Arg Pro Trp Leu Glu Met Gln Ile
  1               5                  10                  15

Asn Ser Asn Gln Ile Pro Gly Leu Ile Trp Ile Asn Lys Glu Glu Met
            20                  25                  30

Ile Phe Gln Ile Pro Trp Lys His Ala Ala Lys His Gly Trp Asp Ile
        35                  40                  45

Asn Lys Asp Ala Cys Leu Phe Arg Ser Trp Ala Ile His Thr Gly Arg
    50                  55                  60

Tyr Lys Ala Gly Glu Lys Glu Pro Asp Pro Lys Thr Trp Lys Ala Asn
65                  70                  75                  80

Phe Arg Cys Ala Met Asn Ser Leu Pro Asp Ile Glu Glu Val Lys Asp
                85                  90                  95

Gln Ser Arg Asn Lys Gly Ser Ser Ala Val Arg Val Tyr Arg Met Leu
```

```
            100                 105                 110

Pro Pro Leu Thr Lys Asn Gln Arg Lys Glu Arg Lys Ser Lys Ser Ser
        115                 120                 125

Arg Asp Ala Lys Ser Lys Ala Lys Arg Lys Ser Cys Gly Asp Ser Ser
    130                 135                 140

Pro Asp Thr Phe Ser Asp Gly Leu Ser Ser Ser Thr Leu Pro Asp Asp
145                 150                 155                 160

His Ser Ser Tyr Thr Val Pro Gly Tyr Met Gln Asp Leu Glu Val Glu
                165                 170                 175

Gln Ala Leu Thr Pro Ala Leu Ser Pro Cys Ala Val Ser Ser Thr Leu
            180                 185                 190

Pro Asp Trp His Ile Pro Val Glu Val Val Pro Asp Ser Thr Ser Asp
        195                 200                 205

Leu Tyr Asn Phe Gln Val Ser Pro Met Pro Ser Thr Ser Glu Ala Thr
    210                 215                 220

Thr Asp Glu Asp Glu Glu Gly Lys Leu Pro Glu Asp Ile Met Lys Leu
225                 230                 235                 240

Leu Glu Gln Ser Glu Trp Gln Pro Thr Asn Val Asp Gly Lys Gly Tyr
                245                 250                 255

Leu Leu Asn Glu Pro Gly Val Gln Pro Thr Ser Val Tyr Gly Asp Phe
            260                 265                 270

Ser Cys Lys Glu Glu Pro Glu Ile Asp Ser Pro Gly Gly Lys Lys Ala
        275                 280                 285

Pro Gly Ser Leu
    290
```

<210> 47
<211> 702
<212> PRT
<213> Homo sapiens

<400> 47

```
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
  1               5                  10                  15

Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Ala Gln
             20                  25                  30

Pro Trp Gly Ala Pro Val Glu Val Glu Ser Phe Leu Val His Pro Gly
         35                  40                  45

Asp Leu Leu Gln Leu Arg Cys Arg Leu Arg Asp Asp Val Gln Ser Ile
     50                  55                  60

Asn Trp Leu Arg Asp Gly Val Gln Leu Ala Glu Ser Asn Arg Thr Arg
 65                  70                  75                  80
```

Ile Thr Gly Glu Glu Val Glu Val Gln Asp Ser Val Pro Ala Asp Ser
85 90 95

Gly Leu Tyr Ala Cys Val Thr Ser Ser Pro Ser Gly Ser Asp Thr Thr
100 105 110

Tyr Phe Ser Val Asn Val Ser Asp Ala Leu Pro Ser Ser Glu Asp Asp
115 120 125

Asp Asp Asp Asp Asp Ser Ser Ser Glu Glu Lys Glu Thr Asp Asn Thr
130 135 140

Lys Pro Asn Arg Met Pro Val Ala Pro Tyr Trp Thr Ser Pro Glu Lys
145 150 155 160

Met Glu Lys Lys Leu His Ala Val Pro Ala Ala Lys Thr Val Lys Phe
165 170 175

Lys Cys Pro Ser Ser Gly Thr Pro Asn Pro Thr Leu Arg Trp Leu Lys
180 185 190

Asn Gly Lys Glu Phe Lys Pro Asp His Arg Ile Gly Gly Tyr Lys Val
195 200 205

Arg Tyr Ala Thr Trp Ser Ile Ile Met Asp Ser Val Val Pro Ser Asp
210 215 220

Lys Gly Asn Tyr Thr Cys Ile Val Glu Asn Glu Tyr Gly Ser Ile Asn
225 230 235 240

His Thr Tyr Gln Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile
245 250 255

Leu Gln Ala Gly Leu Pro Ala Asn Lys Thr Val Ala Leu Gly Ser Asn
260 265 270

Val Glu Phe Met Cys Lys Val Tyr Ser Asp Pro Gln Pro His Ile Gln
275 280 285

Trp Leu Lys His Ile Glu Val Asn Gly Ser Lys Ile Gly Pro Asp Asn
290 295 300

Leu Pro Tyr Val Gln Ile Leu Lys Thr Ala Gly Val Asn Thr Thr Asp
305 310 315 320

Lys Glu Met Glu Val Leu His Leu Arg Asn Val Ser Phe Glu Asp Ala
325 330 335

Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser His His
340 345 350

Ser Ala Trp Leu Thr Val Leu Glu Ala Leu Glu Glu Arg Pro Ala Val
355 360 365

Met Thr Ser Pro Leu Tyr Leu Glu Ile Ile Ile Tyr Cys Thr Gly Ala
370 375 380

Phe Leu Ile Ser Cys Met Val Gly Ser Val Ile Val Tyr Lys Met Lys
385 390 395 400

Ser Gly Thr Lys Lys Ser Asp Phe His Ser Gln Met Ala Val His Lys

405 410 415

Leu Ala Lys Ser Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala Asp
420 425 430

Ser Ser Ala Ser Met Asn Ser Gly Val Leu Leu Val Arg Pro Ser Arg
435 440 445

Leu Ser Ser Ser Gly Thr Pro Met Leu Ala Gly Val Ser Glu Tyr Glu
450 455 460

Leu Pro Glu Asp Pro Arg Trp Glu Leu Pro Arg Asp Arg Leu Val Leu
465 470 475 480

Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val Leu Ala Glu
485 490 495

Ala Ile Gly Leu Asp Lys Asp Lys Pro Asn Arg Val Thr Lys Val Ala
500 505 510

Val Lys Met Leu Lys Ser Asp Ala Thr Glu Lys Asp Leu Ser Asp Leu
515 520 525

Ile Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys Asn Ile
530 535 540

Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val Ile
545 550 555 560

Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Gln Ala Arg
565 570 575

Arg Pro Pro Gly Leu Glu Tyr Cys Tyr Asn Pro Ser His Asn Pro Glu
580 585 590

Glu Gln Leu Ser Ser Lys Asp Leu Val Ser Cys Ala Tyr Gln Val Ala
595 600 605

Arg Gly Met Glu Tyr Leu Ala Ser Lys Lys Cys Ile His Arg Asp Leu
610 615 620

Ala Ala Arg Asn Val Leu Val Thr Glu Asp Asn Val Met Lys Ile Ala
625 630 635 640

Asp Phe Gly Leu Ala Arg Asp Ile His His Ile Asp Tyr Tyr Lys Lys
645 650 655

Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala Leu
660 665 670

Phe Asp Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly Val
675 680 685

Pro His Thr Pro Val Cys Leu Trp Arg Asn Phe Ser Ser Cys
690 695 700

<210> 48
<211> 295
<212> PRT

<213> Homo sapiens

<400> 48

```
Met Pro Lys Arg Gly Lys Lys Gly Ala Val Ala Glu Asp Gly Asp Glu
 1               5                  10                  15

Leu Arg Thr Glu Pro Glu Ala Lys Lys Ser Lys Thr Ala Ala Lys Lys
            20                  25                  30

Asn Asp Lys Glu Ala Ala Gly Glu Gly Pro Ala Leu Tyr Glu Asp Pro
        35                  40                  45

Pro Asp Gln Lys Thr Ser Pro Ser Gly Lys Pro Ala Thr Leu Lys Ile
    50                  55                  60

Cys Ser Trp Asn Val Asp Gly Leu Arg Ala Trp Ile Lys Lys Lys Gly
65                  70                  75                  80

Leu Asp Trp Val Lys Glu Glu Ala Pro Asp Ile Leu Cys Leu Gln Glu
                85                  90                  95

Thr Lys Cys Ser Glu Asn Lys Leu Pro Ala Glu Leu Gln Glu Leu Pro
            100                 105                 110

Gly Leu Ser His Gln Tyr Trp Ser Ala Pro Ser Asp Lys Glu Gly Tyr
        115                 120                 125

Ser Gly Val Gly Leu Leu Ser Arg Gln Cys Pro Leu Lys Val Ser Tyr
    130                 135                 140

Gly Ile Ala Tyr Val Pro Asn Ala Gly Arg Gly Leu Val Arg Leu Glu
145                 150                 155                 160

Tyr Arg Gln Arg Trp Asp Glu Ala Phe Arg Lys Phe Leu Lys Gly Leu
                165                 170                 175

Ala Ser Arg Lys Pro Leu Val Leu Cys Gly Asp Leu Asn Val Ala His
            180                 185                 190

Glu Glu Ile Asp Leu Arg Asn Pro Lys Gly Asn Lys Lys Asn Ala Gly
        195                 200                 205

Phe Thr Pro Gln Glu Arg Gln Gly Phe Gly Glu Leu Leu Gln Ala Val
    210                 215                 220

Pro Leu Ala Asp Ser Phe Arg His Leu Tyr Pro Asn Thr Pro Tyr Ala
225                 230                 235                 240

Tyr Thr Phe Trp Thr Tyr Met Met Asn Ala Arg Ser Lys Asn Val Gly
                245                 250                 255

Trp Arg Leu Asp Tyr Phe Leu Leu Ser His Ser Leu Leu Pro Ala Leu
            260                 265                 270

Cys Asp Ser Lys Ile Arg Ser Lys Ala Leu Gly Ser Asp His Cys Pro
        275                 280                 285

Ile Thr Leu Tyr Leu Ala Leu
    290                 295
```

<210> 49
<211> 342
<212> PRT
<213> Homo sapiens

<400> 49
Met Pro Lys Arg Gly Lys Lys Gly Ala Val Ala Glu Asp Gly Asp Glu
1 5 10 15

Leu Arg Thr Gly Lys Gly Met Lys Ser Ala Leu Leu Pro Arg Asn Cys
20 25 30

Gly Gly Gly Val Cys His Ser Leu Asp Val Arg Glu Pro Glu Ala Lys
35 40 45

Lys Ser Lys Thr Ala Ala Lys Lys Asn Asp Lys Glu Ala Ala Gly Glu
50 55 60

Gly Pro Ala Leu Tyr Glu Asp Pro Pro Asp Gln Lys Thr Ser Pro Ser
65 70 75 80

Gly Lys Pro Ala Thr Leu Lys Ile Cys Ser Trp Asn Val Asp Gly Leu
85 90 95

Arg Ala Trp Ile Lys Lys Lys Gly Leu Asp Trp Val Lys Glu Glu Ala
100 105 110

Pro Asp Ile Leu Cys Leu Gln Glu Thr Lys Cys Ser Glu Asn Lys Leu
115 120 125

Pro Ala Glu Leu Gln Glu Leu Pro Gly Leu Ser His Gln Tyr Trp Ser
130 135 140

Ala Pro Ser Asp Lys Glu Gly Tyr Ser Gly Val Gly Leu Leu Ser Arg
145 150 155 160

Gln Cys Pro Leu Lys Val Ser Tyr Gly Ile Gly Asp Glu Glu His Asp
165 170 175

Gln Glu Gly Arg Val Ile Val Ala Glu Phe Asp Ser Phe Val Leu Val
180 185 190

Thr Ala Tyr Val Pro Asn Ala Gly Arg Gly Leu Val Arg Leu Glu Tyr
195 200 205

Arg Gln Arg Trp Asp Glu Ala Phe Arg Lys Phe Leu Lys Gly Leu Ala
210 215 220

Ser Arg Lys Pro Leu Val Leu Cys Gly Asp Leu Asn Val Ala His Glu
225 230 235 240

Glu Ile Asp Leu Arg Asn Pro Lys Gly Asn Lys Lys Asn Ala Gly Phe
245 250 255

Thr Pro Gln Glu Arg Gln Gly Phe Gly Glu Leu Leu Gln Ala Val Pro
260 265 270

Leu Ala Asp Ser Phe Arg His Leu Tyr Pro Asn Thr Pro Tyr Ala Tyr
275 280 285

```
Thr Phe Trp Thr Tyr Met Met Asn Ala Arg Ser Lys Asn Val Gly Trp
    290                 295                 300

Arg Leu Asp Tyr Phe Leu Leu Ser His Ser Leu Leu Pro Ala Leu Cys
305                 310                 315                 320

Asp Ser Lys Ile Arg Ser Lys Ala Leu Gly Ser Asp His Cys Pro Ile
                325                 330                 335

Thr Leu Tyr Leu Ala Leu
            340
```

<210> 50
<211> 305
<212> PRT
<213> Homo sapiens

<400> 50

```
Met Phe Gln Ala Ala Glu Arg Pro Gln Glu Trp Ala Met Glu Gly Pro
  1               5                  10                  15

Arg Asp Gly Leu Lys Lys Glu Arg Leu Leu Asp Asp Arg His Asp Ser
            20                  25                  30

Gly Leu Asp Ser Met Lys Asp Glu Glu Tyr Glu Gln Met Val Lys Glu
        35                  40                  45

Leu Gln Glu Ile Arg Leu Glu Pro Gln Glu Val Pro Arg Gly Ser Glu
    50                  55                  60

Pro Trp Lys Gln Gln Leu Thr Glu Asp Gly Asp Ser Phe Leu His Leu
65                  70                  75                  80

Ala Ile Ile His Glu Glu Lys Ala Leu Thr Met Glu Val Ile Arg Gln
                85                  90                  95

Val Lys Gly Asp Leu Ala Phe Leu Asn Phe Gln Asn Asn Leu Gln Gln
            100                 105                 110

Thr Pro Leu His Leu Ala Val Ile Thr Asn Gln Pro Glu Ile Ala Glu
        115                 120                 125

Ala Leu Leu Gly Ala Gly Cys Asp Pro Glu Leu Arg Asp Phe Arg Gly
    130                 135                 140

Asn Thr Pro Leu His Leu Ala Cys Glu Gln Gly Cys Leu Ala Ser Val
145                 150                 155                 160

Gly Val Leu Thr Gln Ser Cys Thr Thr Pro His Leu His Ser Ile Leu
                165                 170                 175

Lys Ala Thr Asn Tyr Asn Gly His Thr Cys Leu His Leu Ala Ser Ile
            180                 185                 190

His Gly Tyr Leu Gly Ile Val Glu Leu Leu Val Ser Leu Gly Ala Asp
        195                 200                 205

Val Asn Ala Gln Glu Pro Cys Asn Gly Arg Thr Ala Leu His Leu Ala
    210                 215                 220
```

```
Val Asp Leu Gln Asn Pro Asp Leu Val Ser Leu Leu Leu Lys Cys Gly
225                 230                 235                 240

Ala Asp Val Asn Arg Val Thr Tyr Gln Gly Tyr Ser Pro Tyr Gln Leu
                245                 250                 255

Thr Trp Gly Arg Pro Ser Thr Arg Ile Gln Gln Gln Leu Gly Gln Leu
            260                 265                 270

Thr Leu Glu Asn Leu Gln Met Leu Pro Glu Ser Glu Asp Glu Glu Ser
        275                 280                 285

Tyr Asp Thr Glu Ser Glu Phe Thr Glu Phe Thr Glu Asp Glu Val Ser
    290                 295                 300

Leu
305
```

<210> 51
<211> 289
<212> PRT
<213> Homo sapiens

<400> 51

```
Met Phe Gln Ala Ala Glu Arg Pro Gln Glu Trp Ala Met Glu Gly Pro
  1               5                  10                  15

Arg Asp Gly Leu Lys Lys Glu Arg Leu Leu Asp Asp Arg His Asp Ser
            20                  25                  30

Gly Leu Asp Ser Met Lys Asp Glu Glu Tyr Glu Gln Met Val Lys Glu
        35                  40                  45

Leu Gln Glu Ile Arg Leu Glu Pro Gln Glu Val Pro Arg Gly Ser Glu
    50                  55                  60

Pro Trp Lys Gln Gln Leu Thr Glu Asp Gly Asp Ser Phe Leu His Leu
65                  70                  75                  80

Ala Ile Ile His Glu Glu Lys Ala Leu Thr Met Glu Val Ile Arg Gln
                85                  90                  95

Val Lys Gly Asp Leu Ala Phe Leu Asn Phe Gln Asn Asn Leu Gln Gln
            100                 105                 110

Thr Pro Leu His Leu Ala Val Ile Thr Asn Gln Pro Glu Ile Ala Glu
        115                 120                 125

Ala Leu Leu Gly Ala Gly Cys Asp Pro Glu Leu Arg Asp Phe Arg Gly
    130                 135                 140

Asn Thr Pro Leu His Leu Ala Cys Glu Gln Gly Cys Leu Ala Ser Val
145                 150                 155                 160

Gly Val Leu Thr Gln Ser Cys Thr Thr Pro His Leu His Ser Ile Leu
                165                 170                 175

Lys Ala Thr Asn Tyr Asn Gly Gln Glu Pro Cys Asn Gly Arg Thr Ala
```

```
            180                 185                 190

Leu His Leu Ala Val Asp Leu Gln Asn Pro Asp Leu Val Ser Leu Leu
        195                 200                 205

Leu Lys Cys Gly Ala Asp Val Asn Arg Val Thr Tyr Gln Gly Tyr Ser
    210                 215                 220

Pro Tyr Gln Leu Thr Trp Gly Arg Pro Ser Thr Arg Ile Gln Gln Gln
225                 230                 235                 240

Leu Gly Gln Leu Thr Leu Glu Asn Leu Gln Met Leu Pro Glu Ser Glu
                245                 250                 255

Asp Glu Glu Ser Tyr Asp Thr Glu Ser Glu Phe Thr Glu Phe Thr Glu
            260                 265                 270

Asp Glu Leu Pro Tyr Asp Asp Cys Val Phe Gly Gly Gln Arg Leu Thr
        275                 280                 285

Leu
```

<210> 52
<211> 921
<212> PRT
<213> Homo sapiens

<400> 52

```
Met Ala Gly Ile Phe Tyr Phe Ala Leu Phe Ser Cys Leu Phe Gly Ile
  1               5                  10                  15

Cys Asp Ala Val Thr Gly Ser Arg Val Tyr Pro Ala Asn Glu Val Thr
             20                  25                  30

Leu Leu Asp Ser Arg Ser Val Gln Gly Glu Leu Gly Trp Ile Ala Ser
         35                  40                  45

Pro Leu Glu Gly Gly Trp Glu Glu Val Ser Ile Met Asp Glu Lys Asn
     50                  55                  60

Thr Pro Ile Arg Thr Tyr Gln Val Cys Asn Val Met Glu Pro Ser Gln
 65                  70                  75                  80

Asn Asn Trp Leu Arg Thr Asp Trp Ile Thr Arg Glu Gly Ala Gln Arg
                85                  90                  95

Val Tyr Ile Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro
            100                 105                 110

Gly Val Met Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu
        115                 120                 125

Ser Asp Asn Asp Lys Glu Arg Phe Ile Arg Glu Asn Gln Phe Val Lys
    130                 135                 140

Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Val Asp Ile Gly
145                 150                 155                 160
```

Asp Arg Ile Met Lys Leu Asn Thr Glu Ile Arg Asp Val Gly Pro Leu
165 170 175

Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile
180 185 190

Ala Leu Val Ser Val Arg Val Phe Tyr Lys Lys Cys Pro Leu Thr Val
195 200 205

Arg Asn Leu Ala Gln Phe Pro Asp Thr Ile Thr Gly Ala Asp Thr Ser
210 215 220

Ser Leu Val Glu Val Arg Gly Ser Cys Val Asn Asn Ser Glu Glu Lys
225 230 235 240

Asp Val Pro Lys Met Tyr Cys Gly Ala Asp Gly Glu Trp Leu Val Pro
245 250 255

Ile Gly Asn Cys Leu Cys Asn Ala Gly His Glu Glu Arg Ser Gly Glu
260 265 270

Cys Gln Ala Cys Lys Ile Gly Tyr Tyr Lys Ala Leu Ser Thr Asp Ala
275 280 285

Thr Cys Ala Lys Cys Pro Pro His Ser Tyr Ser Val Trp Glu Gly Ala
290 295 300

Thr Ser Cys Thr Cys Asp Arg Gly Phe Phe Arg Ala Asp Asn Asp Ala
305 310 315 320

Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro Leu Asn Leu Ile
325 330 335

Ser Asn Val Asn Glu Thr Ser Val Asn Leu Glu Trp Ser Ser Pro Gln
340 345 350

Asn Thr Gly Gly Arg Gln Asp Ile Ser Tyr Asn Val Val Cys Lys Lys
355 360 365

Cys Gly Ala Gly Asp Pro Ser Lys Cys Arg Pro Cys Gly Ser Gly Val
370 375 380

His Tyr Thr Pro Gln Gln Asn Gly Leu Lys Thr Thr Lys Val Ser Ile
385 390 395 400

Thr Asp Leu Leu Ala His Thr Asn Tyr Thr Phe Glu Ile Trp Ala Val
405 410 415

Asn Gly Val Ser Lys Tyr Asn Pro Asn Pro Asp Gln Ser Val Ser Val
420 425 430

Thr Val Thr Thr Asn Gln Ala Ala Pro Ser Ser Ile Ala Leu Val Gln
435 440 445

Ala Lys Glu Val Thr Arg Tyr Ser Val Ala Leu Ala Trp Leu Glu Pro
450 455 460

Asp Arg Pro Asn Gly Val Ile Leu Glu Tyr Glu Val Lys Tyr Tyr Glu
465 470 475 480

Lys Asp Gln Asn Glu Arg Ser Tyr Arg Ile Val Arg Thr Ala Ala Arg

485 490 495

Asn Thr Asp Ile Lys Gly Leu Asn Pro Leu Thr Ser Tyr Val Phe His
500 505 510

Val Arg Ala Arg Thr Ala Ala Gly Tyr Gly Asp Phe Ser Glu Pro Leu
515 520 525

Glu Val Thr Thr Asn Thr Val Pro Ser Arg Ile Ile Gly Asp Gly Ala
530 535 540

Asn Ser Thr Val Leu Leu Val Ser Val Ser Gly Ser Val Val Leu Val
545 550 555 560

Val Ile Leu Ile Ala Ala Phe Val Ile Ser Arg Arg Arg Ser Lys Tyr
565 570 575

Ser Lys Ala Lys Gln Glu Ala Asp Glu Glu Lys His Leu Asn Gln Gly
580 585 590

Val Arg Thr Tyr Val Asp Pro Phe Thr Tyr Glu Asp Pro Asn Gln Ala
595 600 605

Val Arg Glu Phe Ala Lys Glu Ile Asp Ala Ser Cys Ile Lys Ile Glu
610 615 620

Lys Val Ile Gly Val Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625 630 635 640

Lys Val Pro Gly Lys Arg Glu Ile Cys Val Ala Ile Lys Thr Leu Lys
645 650 655

Ala Gly Tyr Thr Asp Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
660 665 670

Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu Gly Val
675 680 685

Val Thr Lys Cys Lys Pro Val Met Ile Ile Thr Glu Tyr Met Glu Asn
690 695 700

Gly Ser Leu Asp Ala Phe Leu Arg Lys Asn Asp Gly Arg Phe Thr Val
705 710 715 720

Ile Gln Leu Val Gly Met Leu Arg Gly Ile Gly Ser Gly Met Lys Tyr
725 730 735

Leu Ser Asp Met Ser Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
740 745 750

Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Met Ser
755 760 765

Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
770 775 780

Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785 790 795 800

Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu
805 810 815

```
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830

Pro Asn Thr Ala Leu Leu Asp Pro Ser Ser Pro Glu Phe Ser Ala Val
        835                 840                 845

Val Ser Val Gly Asp Trp Leu Gln Ala Ile Lys Met Asp Arg Tyr Lys
    850                 855                 860

Asp Asn Phe Thr Ala Ala Gly Tyr Thr Thr Leu Glu Ala Val Val His
865                 870                 875                 880

Val Asn Gln Glu Asp Leu Ala Arg Ile Gly Ile Thr Ala Ile Thr His
                885                 890                 895

Gln Asn Lys Ile Leu Ser Ser Val Gln Ala Met Arg Thr Gln Met Gln
            900                 905                 910

Gln Met His Gly Arg Met Val Pro Val
        915                 920
```

<210> 53
<211> 444
<212> PRT
<213> Homo sapiens

<400> 53

```
Met Asn Asp Phe Gly Ile Lys Asn Met Asp Gln Val Ala Pro Val Ala
  1               5                  10                  15

Asn Ser Tyr Arg Gly Thr Leu Lys Arg Gln Pro Ala Phe Asp Thr Phe
            20                  25                  30

Asp Gly Ser Leu Phe Ala Val Phe Pro Ser Leu Asn Glu Glu Gln Thr
        35                  40                  45

Leu Gln Glu Val Pro Thr Gly Leu Asp Ser Ile Ser His Asp Ser Ala
    50                  55                  60

Asn Cys Glu Leu Pro Leu Leu Thr Pro Cys Ser Lys Ala Val Met Ser
65                  70                  75                  80

Gln Ala Leu Lys Ala Thr Phe Ser Gly Phe Phe Trp Ala Thr Asn Glu
                85                  90                  95

Phe Ser Leu Val Asn Val Asn Leu Gln Arg Phe Gly Met Asn Gly Gln
            100                 105                 110

Met Leu Cys Asn Leu Gly Lys Glu Arg Phe Leu Glu Leu Ala Pro Asp
        115                 120                 125

Phe Val Gly Asp Ile Leu Trp Glu His Leu Glu Gln Met Ile Lys Glu
    130                 135                 140

Asn Gln Glu Lys Thr Glu Asp Gln Tyr Glu Glu Asn Ser His Leu Thr
145                 150                 155                 160

Ser Val Pro His Trp Ile Asn Ser Asn Thr Leu Gly Phe Gly Thr Glu
```

```
                165                 170                 175

Gln Ala Pro Tyr Gly Met Gln Thr Gln Asn Tyr Pro Lys Gly Gly Leu
            180                 185                 190

Leu Asp Ser Met Cys Pro Ala Ser Thr Pro Ser Val Leu Ser Ser Glu
        195                 200                 205

Gln Glu Phe Gln Met Phe Pro Lys Ser Arg Leu Ser Ser Val Ser Val
    210                 215                 220

Thr Tyr Cys Ser Val Ser Gln Asp Phe Pro Gly Ser Asn Leu Asn Leu
225                 230                 235                 240

Leu Thr Asn Asn Ser Gly Thr Pro Lys Asp His Asp Ser Pro Glu Asn
                245                 250                 255

Gly Ala Asp Ser Phe Glu Ser Ser Asp Ser Leu Leu Gln Ser Trp Asn
            260                 265                 270

Ser Gln Ser Ser Leu Leu Asp Val Gln Arg Val Pro Ser Phe Glu Ser
        275                 280                 285

Phe Glu Asp Asp Cys Ser Gln Ser Leu Cys Leu Asn Lys Pro Thr Met
    290                 295                 300

Ser Phe Lys Asp Tyr Ile Gln Glu Arg Ser Asp Pro Val Glu Gln Gly
305                 310                 315                 320

Lys Pro Val Ile Pro Ala Ala Val Leu Ala Gly Phe Thr Gly Ser Gly
                325                 330                 335

Pro Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Lys Ser
            340                 345                 350

Cys Gln Ser Phe Ile Ser Trp Thr Gly Asp Gly Trp Glu Phe Lys Leu
        355                 360                 365

Ala Asp Pro Asp Glu Val Ala Arg Arg Trp Gly Lys Arg Lys Asn Lys
    370                 375                 380

Pro Lys Met Asn Tyr Glu Lys Leu Ser Arg Gly Leu Arg Tyr Tyr Tyr
385                 390                 395                 400

Asp Lys Asn Ile Ile His Lys Thr Ser Gly Lys Arg Tyr Val Tyr Arg
                405                 410                 415

Phe Val Cys Asp Leu Gln Asn Leu Leu Gly Phe Thr Pro Glu Glu Leu
            420                 425                 430

His Ala Ile Leu Gly Val Gln Pro Asp Thr Glu Asp
        435                 440
```

<210> 54
<211> 260
<212> PRT
<213> Homo sapiens

<400> 54

```
Met Ala Gly Ser Ala Met Ser Ser Lys Phe Phe Leu Val Ala Leu Ala
 1               5                  10                  15

Ile Phe Phe Ser Phe Ala Gln Val Val Ile Glu Ala Asn Ser Trp Trp
            20                  25                  30

Ser Leu Gly Met Asn Asn Pro Val Gln Met Ser Glu Val Tyr Ile Ile
        35                  40                  45

Gly Ala Gln Pro Leu Cys Ser Gln Leu Ala Gly Leu Ser Gln Gly Gln
    50                  55                  60

Lys Lys Leu Cys His Leu Tyr Gln Asp His Met Gln Tyr Ile Gly Glu
65                  70                  75                  80

Gly Ala Lys Thr Gly Ile Lys Glu Cys Gln Tyr Gln Phe Arg His Arg
                85                  90                  95

Arg Trp Asn Cys Ser Thr Val Asp Asn Thr Ser Val Phe Gly Arg Val
            100                 105                 110

Met Gln Ile Gly Ser Arg Glu Thr Ala Phe Thr Tyr Ala Val Ser Ala
        115                 120                 125

Ala Gly Val Val Asn Ala Met Ser Arg Ala Cys Arg Glu Gly Glu Leu
    130                 135                 140

Ser Thr Cys Gly Cys Ser Arg Ala Ala Arg Pro Lys Asp Leu Pro Arg
145                 150                 155                 160

Asp Trp Leu Trp Gly Gly Cys Gly Asp Asn Ile Asp Tyr Gly Tyr Arg
                165                 170                 175

Phe Ala Lys Glu Phe Val Asp Ala Arg Glu Arg Glu Arg Ile His Ala
            180                 185                 190

Lys Gly Ser Tyr Glu Ser Ala Arg Ile Leu Met Asn Leu His Asn Asn
        195                 200                 205

Glu Ala Gly Arg Arg Thr Val Tyr Asn Leu Ala Asp Val Ala Cys Lys
    210                 215                 220

Cys His Gly Val Ser Gly Ser Cys Ser Leu Lys Thr Cys Trp Leu Gln
225                 230                 235                 240

Leu Ala Asp Phe Arg Lys Val Gly Asp Ala Leu Lys Glu Lys Tyr Asp
                245                 250                 255

Thr Leu Val Gly
            260
```

<210> 55
<211> 719
<212> PRT
<213> Homo sapiens

<400> 55

```
Met Ala Leu Arg Arg Ser Met Gly Arg Pro Gly Leu Pro Pro Leu Pro
 1               5                  10                  15
```

```
Leu Pro Pro Pro Pro Arg Leu Gly Leu Leu Leu Ala Glu Ser Ala Ala
            20                  25                  30

Ala Gly Leu Lys Leu Met Gly Ala Pro Val Lys Leu Thr Val Ser Gln
        35                  40                  45

Gly Gln Pro Val Lys Leu Asn Cys Ser Val Glu Gly Met Glu Glu Pro
    50                  55                  60

Asp Ile Gln Trp Val Lys Asp Gly Ala Val Val Gln Asn Leu Asp Gln
65                  70                  75                  80

Leu Tyr Ile Pro Val Ser Glu Gln His Trp Ile Gly Phe Leu Ser Leu
                85                  90                  95

Lys Ser Val Glu Arg Ser Asp Ala Gly Arg Tyr Trp Cys Gln Val Glu
            100                 105                 110

Asp Gly Gly Glu Thr Glu Ile Ser Gln Pro Val Trp Leu Thr Val Glu
        115                 120                 125

Gly Val Pro Phe Phe Thr Val Glu Pro Lys Asp Leu Ala Val Pro Pro
    130                 135                 140

Asn Ala Pro Phe Gln Leu Ser Cys Glu Ala Val Gly Pro Pro Glu Pro
145                 150                 155                 160

Val Thr Ile Val Trp Trp Arg Gly Thr Thr Lys Ile Gly Gly Pro Ala
                165                 170                 175

Pro Ser Pro Ser Val Leu Asn Val Thr Gly Val Thr Gln Ser Thr Met
            180                 185                 190

Phe Ser Cys Glu Ala His Asn Leu Lys Gly Leu Ala Ser Ser Arg Thr
        195                 200                 205

Ala Thr Val His Leu Gln Ala Leu Pro Ala Ala Pro Phe Asn Ile Thr
    210                 215                 220

Val Thr Lys Leu Ser Ser Ser Asn Ala Ser Val Ala Trp Met Pro Gly
225                 230                 235                 240

Ala Asp Gly Arg Ala Leu Leu Gln Ser Cys Thr Val Gln Val Thr Gln
                245                 250                 255

Ala Pro Gly Gly Trp Glu Val Leu Ala Val Val Val Pro Val Pro Pro
            260                 265                 270

Phe Thr Cys Leu Leu Arg Asp Leu Val Pro Ala Thr Asn Tyr Ser Leu
        275                 280                 285

Arg Val Arg Cys Ala Asn Ala Leu Gly Pro Ser Pro Tyr Ala Asp Trp
    290                 295                 300

Val Pro Phe Gln Thr Lys Gly Leu Ala Pro Ala Ser Ala Pro Gln Asn
305                 310                 315                 320

Leu His Ala Ile Arg Thr Asp Ser Gly Leu Ile Leu Glu Trp Glu Glu
                325                 330                 335
```

Val Ile Pro Glu Ala Pro Leu Glu Gly Pro Leu Gly Pro Tyr Lys Leu
340 345 350

Ser Trp Val Gln Asp Asn Gly Thr Gln Asp Glu Leu Thr Val Glu Gly
355 360 365

Thr Arg Ala Asn Leu Thr Gly Trp Asp Pro Gln Lys Asp Leu Ile Val
370 375 380

Arg Val Cys Val Ser Asn Ala Val Gly Cys Gly Pro Trp Ser Gln Pro
385 390 395 400

Leu Val Val Ser Ser His Asp Arg Ala Gly Gln Gln Gly Pro Pro His
405 410 415

Ser Arg Thr Ser Trp Val Pro Val Val Leu Gly Val Leu Thr Ala Leu
420 425 430

Val Thr Ala Ala Ala Leu Ala Leu Ile Leu Leu Arg Lys Arg Arg Lys
435 440 445

Glu Thr Arg Phe Gly Gln Ala Phe Asp Ser Val Met Ala Arg Gly Glu
450 455 460

Pro Ala Val His Phe Arg Ala Ala Arg Ser Phe Asn Arg Glu Arg Pro
465 470 475 480

Glu Arg Ile Glu Ala Thr Leu Asp Ser Leu Gly Ile Ser Asp Glu Leu
485 490 495

Lys Glu Lys Leu Glu Asp Val Leu Ile Pro Glu Gln Gln Phe Thr Leu
500 505 510

Gly Arg Met Leu Gly Lys Gly Glu Phe Gly Ser Val Arg Glu Ala Gln
515 520 525

Leu Lys Gln Glu Asp Gly Ser Phe Val Lys Val Ala Val Lys Met Leu
530 535 540

Lys Ala Asp Ile Ile Ala Ser Ser Asp Ile Glu Glu Phe Leu Arg Glu
545 550 555 560

Ala Ala Cys Met Lys Glu Phe Asp His Pro His Val Ala Lys Leu Val
565 570 575

Gly Val Ser Leu Arg Ser Arg Ala Lys Gly Arg Leu Pro Ile Pro Met
580 585 590

Val Ile Leu Pro Phe Met Lys His Gly Asp Leu His Ala Phe Leu Leu
595 600 605

Ala Ser Arg Ile Gly Glu Asn Pro Phe Asn Leu Pro Leu Gln Thr Leu
610 615 620

Ile Arg Phe Met Val Asp Ile Ala Cys Gly Met Glu Tyr Leu Ser Ser
625 630 635 640

Arg Asn Phe Ile His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Ala
645 650 655

Glu Asp Met Thr Val Cys Val Ala Asp Phe Gly Leu Ser Arg Lys Ile

660 665 670

Tyr Ser Asp Cys Arg Tyr Ile Leu Thr Pro Gly Gly Leu Ala Glu Gln
675 680 685

Pro Gly Gln Ala Glu His Gln Pro Glu Ser Pro Leu Asn Glu Thr Gln
690 695 700

Arg Leu Leu Leu Leu Gln Gln Gly Leu Leu Pro His Ser Ser Cys
705 710 715

<210> 56
<211> 848
<212> PRT
<213> Homo sapiens

<400> 56
Met Cys Arg Ile Ala Gly Ala Leu Arg Thr Leu Leu Pro Leu Leu Ala
1 5 10 15

Ala Leu Leu Gln Ala Ser Val Glu Ala Ser Gly Glu Ile Ala Leu Cys
20 25 30

Lys Thr Gly Phe Pro Glu Asp Val Tyr Ser Ala Val Leu Ser Lys Asp
35 40 45

Val His Glu Gly Gln Pro Leu Leu Asn Val Lys Phe Ser Asn Cys Asn
50 55 60

Gly Lys Arg Lys Val Gln Tyr Glu Ser Ser Glu Pro Ala Asp Phe Lys
65 70 75 80

Val Asp Glu Asp Gly Met Val Tyr Ala Val Arg Ser Phe Pro Leu Ser
85 90 95

Ser Glu His Ala Lys Phe Leu Ile Tyr Ala Gln Asp Lys Glu Thr Gln
100 105 110

Glu Lys Trp Gln Val Ala Val Lys Leu Ser Leu Lys Pro Thr Leu Thr
115 120 125

Glu Glu Ser Val Lys Glu Ser Ala Glu Val Glu Glu Ile Val Phe Pro
130 135 140

Arg Gln Phe Ser Lys His Ser Gly His Leu Gln Arg Gln Lys Arg Asp
145 150 155 160

Trp Val Ile Pro Pro Ile Asn Leu Pro Glu Asn Ser Arg Gly Pro Phe
165 170 175

Pro Gln Glu Leu Val Arg Ile Arg Ser Asp Arg Asp Lys Asn Leu Ser
180 185 190

Leu Arg Tyr Ser Val Thr Gly Pro Gly Ala Asp Gln Pro Pro Thr Gly
195 200 205

Ile Phe Ile Ile Asn Pro Ile Ser Gly Gln Leu Ser Val Thr Lys Pro
210 215 220

```
Leu Asp Arg Glu Gln Ile Ala Arg Phe His Leu Arg Ala His Ala Val
225                 230                 235                 240

Asp Ile Asn Gly Asn Gln Val Glu Asn Pro Ile Asp Ile Val Ile Asn
                245                 250                 255

Val Ile Asp Met Asn Asp Asn Arg Pro Glu Phe Leu His Gln Val Trp
            260                 265                 270

Asn Gly Thr Val Pro Glu Gly Ser Lys Pro Gly Thr Tyr Val Met Thr
        275                 280                 285

Val Thr Ala Ile Asp Ala Asp Asp Pro Asn Ala Leu Asn Gly Met Leu
    290                 295                 300

Arg Tyr Arg Ile Val Ser Gln Ala Pro Ser Thr Pro Ser Pro Asn Met
305                 310                 315                 320

Phe Thr Ile Asn Asn Glu Thr Gly Asp Ile Ile Thr Val Ala Ala Gly
                325                 330                 335

Leu Asp Arg Glu Lys Val Gln Gln Tyr Thr Leu Ile Ile Gln Ala Thr
            340                 345                 350

Asp Met Glu Gly Asn Pro Thr Tyr Gly Leu Ser Asn Thr Ala Thr Ala
        355                 360                 365

Val Ile Thr Val Thr Asp Val Asn Asp Asn Pro Pro Glu Phe Thr Ala
    370                 375                 380

Met Thr Phe Tyr Gly Glu Val Pro Glu Asn Arg Val Asp Ile Ile Val
385                 390                 395                 400

Ala Asn Leu Thr Val Thr Asp Lys Asp Gln Pro His Thr Pro Ala Trp
                405                 410                 415

Asn Ala Val Tyr Arg Ile Ser Gly Gly Asp Pro Thr Gly Arg Phe Ala
            420                 425                 430

Ile Gln Thr Asp Pro Asn Ser Asn Asp Gly Leu Val Thr Val Val Lys
        435                 440                 445

Pro Ile Asp Phe Glu Thr Asn Arg Met Phe Val Leu Thr Val Ala Ala
    450                 455                 460

Glu Asn Gln Val Pro Leu Ala Lys Gly Ile Gln His Pro Pro Gln Ser
465                 470                 475                 480

Thr Ala Thr Val Ser Val Thr Val Ile Asp Val Asn Glu Asn Pro Tyr
                485                 490                 495

Phe Ala Pro Asn Pro Lys Ile Ile Arg Gln Glu Glu Gly Leu His Ala
            500                 505                 510

Gly Thr Met Leu Thr Thr Phe Thr Ala Gln Asp Pro Asp Arg Tyr Met
        515                 520                 525

Gln Gln Asn Ile Arg Tyr Thr Lys Leu Ser Asp Pro Ala Asn Trp Leu
    530                 535                 540

Lys Ile Asp Pro Val Asn Gly Gln Ile Thr Thr Ile Ala Val Leu Asp
```

545 550 555 560

Arg Glu Ser Pro Asn Val Lys Asn Asn Ile Tyr Asn Ala Thr Phe Leu
565 570 575

Ala Ser Asp Asn Gly Ile Pro Pro Met Ser Gly Thr Gly Thr Leu Gln
580 585 590

Ile Tyr Leu Leu Asp Ile Asn Asp Asn Ala Pro Gln Val Leu Pro Gln
595 600 605

Glu Ala Glu Thr Cys Glu Thr Pro Asp Pro Asn Ser Ile Asn Ile Thr
610 615 620

Ala Leu Asp Tyr Asp Ile Asp Pro Asn Ala Gly Pro Phe Ala Phe Asp
625 630 635 640

Leu Pro Leu Ser Pro Val Thr Ile Lys Arg Asn Trp Thr Ile Thr Arg
645 650 655

Leu Asn Gly Asp Phe Ala Gln Leu Asn Leu Lys Ile Lys Phe Leu Glu
660 665 670

Ala Gly Ile Tyr Glu Val Pro Ile Ile Ile Thr Asp Ser Gly Asn Pro
675 680 685

Pro Lys Ser Asn Ile Ser Ile Leu Arg Val Lys Val Cys Gln Cys Asp
690 695 700

Ser Asn Gly Asp Cys Thr Asp Val Asp Arg Ile Val Gly Ala Gly Leu
705 710 715 720

Gly Thr Gly Ala Ile Ile Ala Ile Leu Leu Cys Ile Ile Ile Leu Leu
725 730 735

Ile Leu Val Leu Met Phe Val Val Trp Met Lys Arg Arg Asp Lys Glu
740 745 750

Arg Gln Ala Lys Gln Leu Leu Ile Asp Pro Glu Asp Asp Val Arg Asp
755 760 765

Asn Ile Leu Lys Tyr Asp Glu Glu Gly Gly Gly Glu Glu Asp Gln Asp
770 775 780

Tyr Asp Leu Ser Gln Leu Gln Gln Pro Asp Thr Val Glu Pro Asp Ala
785 790 795 800

Ile Lys Pro Val Gly Ile Arg Arg Met Asp Glu Arg Pro Ile His Ala
805 810 815

Glu Pro Gln Tyr Pro Val Arg Ser Ala Ala Pro His Pro Gly Asp Ile
820 825 830

Gly Asp Phe Ile Asn Glu Lys Thr Trp Pro Ile Gln Ser Leu His Leu
835 840 845

<210> 57
<211> 103
<212> PRT
<213> Homo sapiens

<400> 57
Met Glu Arg Val Lys Met Ile Asn Val Gln Arg Leu Leu Glu Ala Ala
1 5 10 15

Glu Phe Leu Glu Arg Arg Glu Arg Glu Cys Glu His Gly Tyr Ala Ser
20 25 30

Ser Phe Pro Ser Met Pro Ser Pro Arg Leu Gln His Ser Lys Pro Pro
35 40 45

Arg Arg Leu Ser Arg Ala Gln Lys His Ser Ser Gly Ser Ser Asn Thr
50 55 60

Ser Thr Ala Asn Arg Ser Thr His Asn Glu Leu Glu Lys Asn Arg Leu
65 70 75 80

Lys Asn Trp Leu Val Gly Arg Arg Asp Thr Arg Gly Met Lys Met Leu
85 90 95

Leu Lys Ala Ile Ala Val Ile
100

<210> 58
<211> 234
<212> PRT
<213> Homo sapiens

<400> 58
Met Glu Lys His Ile Asn Thr Phe Leu Gln Asn Val Gln Ile Leu Leu
1 5 10 15

Glu Ala Ala Ser Tyr Leu Glu Gln Ile Glu Lys Glu Asn Lys Lys Cys
20 25 30

Glu His Gly Tyr Ala Ser Ser Phe Pro Ser Met Pro Ser Pro Arg Leu
35 40 45

Gln His Ser Lys Pro Pro Arg Arg Leu Ser Arg Ala Gln Lys His Ser
50 55 60

Ser Gly Ser Ser Asn Thr Ser Thr Ala Asn Arg Ser Thr His Asn Glu
65 70 75 80

Leu Glu Lys Asn Arg Arg Ala His Leu Arg Leu Cys Leu Glu Arg Leu
85 90 95

Lys Val Leu Ile Pro Leu Gly Pro Asp Cys Thr Arg His Thr Thr Leu
100 105 110

Gly Leu Leu Asn Lys Ala Lys Ala His Ile Lys Lys Leu Glu Glu Ala
115 120 125

Glu Arg Lys Ser Gln His Gln Leu Glu Asn Leu Glu Arg Glu Gln Arg
130 135 140

```
Phe Leu Lys Trp Arg Leu Glu Gln Leu Gln Gly Pro Gln Glu Met Glu
145                 150                 155                 160

Arg Ile Arg Met Asp Ser Ile Gly Ser Thr Ile Ser Ser Asp Arg Ser
                165                 170                 175

Asp Ser Glu Arg Glu Glu Ile Glu Val Asp Val Glu Ser Thr Glu Phe
            180                 185                 190

Ser His Gly Glu Val Asp Asn Ile Ser Thr Thr Ser Ile Ser Asp Ile
        195                 200                 205

Asp Asp His Ser Ser Leu Pro Ser Ile Gly Ser Asp Glu Gly Tyr Ser
    210                 215                 220

Ser Ala Ser Val Lys Leu Ser Phe Thr Ser
225                 230
```

<210> 59
<211> 329
<212> PRT
<213> Homo sapiens

<400> 59

```
Met Glu Ser Pro Ala Ser Ser Gln Pro Ala Ser Met Pro Gln Ser Lys
  1                 5                  10                  15

Gly Lys Ser Lys Arg Lys Lys Asp Leu Arg Ile Ser Cys Met Ser Lys
             20                  25                  30

Pro Pro Ala Pro Asn Pro Thr Pro Pro Arg Asn Leu Asp Ser Arg Thr
         35                  40                  45

Phe Ile Thr Ile Gly Asp Arg Asn Phe Glu Val Glu Ala Asp Asp Leu
     50                  55                  60

Val Thr Ile Ser Glu Leu Gly Arg Gly Ala Tyr Gly Val Val Glu Lys
 65                  70                  75                  80

Val Arg His Ala Gln Ser Gly Thr Ile Met Ala Val Lys Arg Ile Arg
                 85                  90                  95

Ala Thr Val Asn Ser Gln Glu Gln Lys Arg Leu Leu Met Asp Leu Asp
            100                 105                 110

Ile Asn Met Arg Thr Val Asp Cys Phe Tyr Thr Val Thr Phe Tyr Gly
        115                 120                 125

Ala Leu Phe Arg Glu Gly Asp Val Trp Ile Cys Met Glu Leu Met Asp
    130                 135                 140

Thr Ser Leu Asp Lys Phe Tyr Arg Lys Val Leu Asp Lys Asn Met Thr
145                 150                 155                 160

Ile Pro Glu Asp Ile Leu Gly Glu Ile Ala Val Ser Ile Val Arg Ala
                165                 170                 175

Leu Glu His Leu His Ser Lys Leu Ser Val Ile His Arg Asp Val Lys
```

```
            180                 185                 190

Pro Ser Asn Val Leu Ile Asn Lys Glu Gly His Val Lys Met Cys Asp
        195                 200                 205

Phe Gly Ile Ser Gly Tyr Leu Val Asp Ser Val Ala Lys Thr Met Asp
    210                 215                 220

Ala Gly Cys Lys Pro Tyr Met Ala Pro Glu Arg Ile Asn Pro Glu Leu
225                 230                 235                 240

Asn Gln Lys Gly Tyr Asn Val Lys Ser Asp Val Trp Ser Leu Gly Ile
                245                 250                 255

Thr Met Ile Glu Met Ala Ile Leu Arg Phe Pro Tyr Glu Ser Trp Gly
            260                 265                 270

Thr Pro Phe Gln Gln Leu Lys Gln Val Val Glu Glu Pro Ser Pro Gln
        275                 280                 285

Leu Pro Ala Asp Arg Phe Ser Pro Glu Phe Val Asp Phe Thr Ala Gln
    290                 295                 300

Cys Leu Arg Lys Asn Pro Ala Glu Arg Met Ser Tyr Leu Glu Leu Ile
305                 310                 315                 320

Gly Ala Asp Arg Phe Ser Pro Thr Pro
                325
```

<210> 60
<211> 292
<212> PRT
<213> Homo sapiens

<400> 60

```
Met Pro Glu Ile Arg Leu Arg His Val Val Ser Cys Ser Ser Gln Asp
  1               5                  10                  15

Ser Thr His Cys Ala Glu Asn Leu Leu Lys Ala Asp Thr Tyr Arg Lys
             20                  25                  30

Trp Arg Ala Ala Lys Ala Gly Glu Lys Thr Ile Ser Val Val Leu Gln
         35                  40                  45

Leu Glu Lys Glu Glu Gln Ile His Ser Val Asp Ile Gly Asn Asp Gly
     50                  55                  60

Ser Ala Phe Val Glu Val Leu Val Gly Ser Ser Ala Gly Gly Ala Gly
 65                  70                  75                  80

Glu Gln Asp Tyr Glu Val Leu Leu Val Thr Ser Ser Phe Met Ser Pro
                 85                  90                  95

Ser Glu Ser Arg Ser Gly Ser Asn Pro Asn Arg Val Arg Met Phe Gly
            100                 105                 110

Pro Asp Lys Leu Val Arg Ala Ala Ala Glu Lys Arg Trp Asp Arg Val
        115                 120                 125
```

```
Lys Ile Val Cys Ser Gln Pro Tyr Ser Lys Asp Ser Pro Phe Gly Leu
    130                 135                 140

Ser Phe Val Arg Phe His Ser Pro Pro Asp Lys Asp Glu Ala Glu Ala
145                 150                 155                 160

Pro Ser Gln Lys Val Thr Val Thr Lys Leu Gly Gln Phe Arg Val Lys
                165                 170                 175

Glu Glu Asp Glu Ser Ala Asn Ser Leu Arg Pro Gly Ala Leu Phe Phe
            180                 185                 190

Ser Arg Ile Asn Lys Thr Ser Pro Val Thr Ala Ser Asp Pro Ala Gly
        195                 200                 205

Pro Ser Tyr Ala Ala Ala Thr Leu Gln Ala Ser Ser Ala Ala Ser Ser
    210                 215                 220

Ala Ser Pro Val Ser Arg Ala Ile Gly Ser Thr Ser Lys Pro Gln Glu
225                 230                 235                 240

Ser Pro Trp His Ser Phe Val Pro Asp Gly Ser Thr Val Ala Met Arg
                245                 250                 255

Ser Arg Ser Tyr Phe Leu Thr Ser Ser Met Gly Trp Cys Arg Lys Pro
            260                 265                 270

Glu Val Cys Ala Ile His Thr His Thr His Thr His Thr His Thr His
        275                 280                 285

Thr Arg Cys Ile
    290
```

<210> 61
<211> 266
<212> PRT
<213> Homo sapiens

<400> 61

```
Met Pro Glu Ile Arg Leu Arg His Val Val Ser Cys Ser Ser Gln Asp
  1               5                  10                  15

Ser Thr His Cys Ala Glu Asn Leu Leu Lys Ala Asp Thr Tyr Arg Lys
            20                  25                  30

Trp Arg Ala Ala Lys Ala Gly Glu Lys Thr Ile Ser Val Val Leu Gln
        35                  40                  45

Leu Glu Lys Glu Glu Gln Ile His Ser Val Asp Ile Gly Asn Asp Gly
    50                  55                  60

Ser Ala Phe Val Glu Val Leu Val Gly Ser Ser Ala Gly Gly Ala Gly
65                  70                  75                  80

Glu Gln Asp Tyr Glu Val Leu Leu Val Thr Ser Ser Phe Met Ser Pro
                85                  90                  95

Ser Glu Ser Arg Ser Gly Ser Asn Pro Asn Arg Val Arg Met Phe Gly
            100                 105                 110
```

```
Pro Asp Lys Leu Val Arg Ala Ala Ala Glu Lys Arg Trp Asp Arg Val
        115                 120                 125

Lys Ile Val Cys Ser Gln Pro Tyr Ser Lys Asp Ser Pro Phe Gly Leu
    130                 135                 140

Ser Phe Val Arg Phe His Ser Pro Pro Asp Lys Asp Glu Ala Glu Ala
145                 150                 155                 160

Pro Ser Gln Lys Val Thr Val Thr Lys Leu Gly Gln Phe Arg Val Lys
                165                 170                 175

Glu Glu Asp Glu Ser Ala Asn Ser Leu Arg Pro Gly Ala Leu Phe Phe
            180                 185                 190

Ser Arg Ile Asn Lys Thr Ser Pro Val Thr Ala Ser Asp Pro Ala Gly
        195                 200                 205

Pro Ser Tyr Ala Ala Ala Thr Leu Gln Ala Ser Ser Ala Ala Ser Ser
    210                 215                 220

Ala Ser Pro Val Ser Arg Ala Ile Gly Ser Thr Ser Lys Pro Gln Glu
225                 230                 235                 240

Ser Ser Asp Phe Gly Gly Val Glu Glu Glu Arg Ser Trp Arg Pro Gln
                245                 250                 255

Ser Ile Pro Ile Pro Ser Ala Pro Gly Ser
            260                 265
```

<210> 62
<211> 247
<212> PRT
<213> Homo sapiens

<400> 62

```
Met Pro Glu Ile Arg Leu Arg His Val Val Ser Cys Ser Ser Gln Asp
  1               5                  10                  15

Ser Thr His Cys Ala Glu Asn Leu Leu Lys Ala Asp Thr Tyr Arg Lys
            20                  25                  30

Trp Arg Ala Ala Lys Ala Gly Glu Lys Thr Ile Ser Val Val Leu Gln
        35                  40                  45

Leu Glu Lys Glu Glu Gln Ile His Ser Val Asp Ile Gly Asn Asp Gly
    50                  55                  60

Ser Ala Phe Val Glu Val Leu Val Gly Ser Ser Ala Gly Gly Ala Gly
65                  70                  75                  80

Glu Gln Asp Tyr Glu Val Leu Leu Val Thr Ser Ser Phe Met Ser Pro
                85                  90                  95

Ser Glu Ser Arg Ser Gly Ser Asn Pro Asn Arg Val Arg Met Phe Gly
            100                 105                 110

Pro Asp Lys Leu Val Arg Ala Ala Ala Glu Lys Arg Trp Asp Arg Val
```

```
       115                 120                 125

Lys Ile Val Cys Ser Gln Pro Tyr Ser Lys Asp Ser Pro Phe Gly Leu
    130                 135                 140

Ser Phe Val Arg Phe His Ser Pro Pro Asp Lys Asp Glu Ala Glu Ala
145                 150                 155                 160

Pro Ser Gln Lys Val Thr Val Thr Lys Leu Gly Gln Phe Arg Val Lys
                165                 170                 175

Glu Glu Asp Glu Ser Ala Asn Ser Leu Arg Leu Glu Asp Tyr Met Ser
            180                 185                 190

Asp Arg Val Gln Phe Val Ile Thr Ala Gln Glu Trp Asp Pro Ser Phe
        195                 200                 205

Glu Glu Ala Leu Met Asp Asn Pro Ser Leu Ala Phe Val Arg Pro Arg
    210                 215                 220

Trp Ile Tyr Ser Cys Asn Glu Lys Gln Lys Leu Leu Pro His Gln Leu
225                 230                 235                 240

Tyr Gly Val Val Pro Gln Ala
                245
```

<210> 63
<211> 624
<212> PRT
<213> Homo sapiens

<400> 63

```
Met Pro Glu Ile Arg Leu Arg His Val Val Ser Cys Ser Ser Gln Asp
  1               5                  10                  15

Ser Thr His Cys Ala Glu Asn Leu Leu Lys Ala Asp Thr Tyr Arg Lys
            20                  25                  30

Trp Arg Ala Ala Lys Ala Gly Glu Lys Thr Ile Ser Val Val Leu Gln
        35                  40                  45

Leu Glu Lys Glu Glu Gln Ile His Ser Val Asp Ile Gly Asn Asp Gly
    50                  55                  60

Ser Ala Phe Val Glu Val Leu Val Gly Ser Ser Ala Gly Gly Ala Gly
65                  70                  75                  80

Glu Gln Asp Tyr Glu Val Leu Leu Val Thr Ser Ser Phe Met Ser Pro
                85                  90                  95

Ser Glu Ser Arg Ser Gly Ser Asn Pro Asn Arg Val Arg Met Phe Gly
            100                 105                 110

Pro Asp Lys Leu Val Arg Ala Ala Ala Glu Lys Arg Trp Asp Arg Val
        115                 120                 125

Lys Ile Val Cys Ser Gln Pro Tyr Ser Lys Asp Ser Pro Phe Gly Leu
    130                 135                 140
```

```
Ser Phe Val Arg Phe His Ser Pro Pro Asp Lys Asp Glu Ala Glu Ala
145                 150                 155                 160

Pro Ser Gln Lys Val Thr Val Thr Lys Leu Gly Gln Phe Arg Val Lys
                165                 170                 175

Glu Glu Asp Glu Ser Ala Asn Ser Leu Arg Pro Gly Ala Leu Phe Phe
            180                 185                 190

Ser Arg Ile Asn Lys Thr Ser Pro Val Thr Ala Ser Asp Pro Ala Gly
        195                 200                 205

Pro Ser Tyr Ala Ala Ala Thr Leu Gln Ala Ser Ser Ala Ala Ser Ser
    210                 215                 220

Ala Ser Pro Val Ser Arg Ala Ile Gly Ser Thr Ser Lys Pro Gln Glu
225                 230                 235                 240

Ser Pro Lys Gly Lys Arg Lys Leu Asp Leu Asn Gln Glu Glu Lys Lys
                245                 250                 255

Thr Pro Ser Lys Pro Pro Ala Gln Leu Ser Pro Ser Val Pro Lys Arg
            260                 265                 270

Pro Lys Leu Pro Ala Pro Thr Arg Thr Pro Ala Thr Ala Pro Val Pro
        275                 280                 285

Ala Arg Ala Gln Gly Ala Val Thr Gly Lys Pro Arg Gly Glu Gly Thr
    290                 295                 300

Glu Pro Arg Arg Pro Arg Ala Gly Pro Glu Glu Leu Gly Lys Ile Leu
305                 310                 315                 320

Gln Gly Val Val Val Val Leu Ser Gly Phe Gln Asn Pro Phe Arg Ser
                325                 330                 335

Glu Leu Arg Asp Lys Ala Leu Glu Leu Gly Ala Lys Tyr Arg Pro Asp
            340                 345                 350

Trp Thr Arg Asp Ser Thr His Leu Ile Cys Ala Phe Ala Asn Thr Pro
        355                 360                 365

Lys Tyr Ser Gln Val Leu Gly Leu Gly Gly Arg Ile Val Arg Lys Glu
    370                 375                 380

Trp Val Leu Asp Cys His Arg Met Arg Arg Arg Leu Pro Ser Arg Arg
385                 390                 395                 400

Tyr Leu Met Ala Gly Pro Gly Ser Ser Ser Glu Glu Asp Glu Ala Ser
                405                 410                 415

His Ser Gly Gly Ser Gly Asp Glu Ala Pro Lys Leu Pro Gln Lys Gln
            420                 425                 430

Pro Gln Thr Lys Thr Lys Pro Thr Gln Ala Ala Gly Pro Ser Ser Pro
        435                 440                 445

Gln Lys Pro Pro Thr Pro Glu Glu Thr Lys Ala Ala Ser Pro Val Leu
    450                 455                 460

Gln Glu Asp Ile Asp Ile Glu Gly Val Gln Ser Glu Gly Gln Asp Asn
```

```
465                 470                 475                 480

Gly Ala Glu Asp Ser Gly Asp Thr Glu Asp Glu Leu Arg Arg Val Ala
                485                 490                 495

Glu Gln Lys Glu His Arg Leu Pro Pro Gly Gln Glu Glu Asn Gly Glu
            500                 505                 510

Asp Pro Tyr Ala Gly Ser Thr Asp Glu Asn Thr Asp Ser Glu Glu His
        515                 520                 525

Gln Glu Pro Pro Asp Leu Pro Val Pro Glu Leu Pro Arg Phe Leu Pro
    530                 535                 540

Gly Gln Ala Leu Leu Ser Leu Arg Gly Val Pro Trp Gly Arg Ala Ala
545                 550                 555                 560

Glu Thr His Pro Ile Arg His Ser Leu Gln Trp Gly Ala Pro Trp His
                565                 570                 575

Ser Phe Val Pro Asp Gly Ser Thr Val Ala Met Arg Ser Arg Ser Tyr
            580                 585                 590

Phe Leu Thr Ser Ser Met Gly Trp Cys Arg Lys Pro Glu Val Cys Ala
        595                 600                 605

Ile His Thr His Thr His Thr His Thr His Thr His Thr Arg Cys Ile
    610                 615                 620
```

<210> 64
<211> 567
<212> PRT
<213> Homo sapiens

<400> 64

```
Met Ala Gly Ala Ile Ala Ser Arg Met Ser Phe Ser Ser Leu Lys Arg
  1               5                  10                  15

Lys Gln Pro Lys Thr Phe Thr Val Arg Ile Val Thr Met Asp Ala Glu
             20                  25                  30

Met Glu Phe Asn Cys Glu Met Lys Trp Lys Gly Lys Asp Leu Phe Asp
         35                  40                  45

Leu Val Cys Arg Thr Leu Gly Leu Arg Glu Thr Trp Phe Phe Gly Leu
     50                  55                  60

Gln Tyr Thr Ile Lys Asp Thr Val Ala Trp Leu Lys Met Asp Lys Lys
 65                  70                  75                  80

Val Leu Asp His Asp Val Ser Lys Glu Glu Pro Val Thr Phe His Phe
                85                  90                  95

Leu Ala Lys Phe Tyr Pro Glu Asn Ala Glu Glu Glu Leu Val Gln Glu
            100                 105                 110
```

```
Ile Thr Gln His Leu Phe Phe Leu Gln Val Lys Lys Gln Ile Leu Asp
        115                 120                 125

Glu Lys Ile Tyr Cys Pro Pro Glu Ala Ser Val Leu Leu Ala Ser Tyr
    130                 135                 140

Ala Val Gln Ala Lys Tyr Gly Asp Tyr Asp Pro Ser Val His Lys Arg
145                 150                 155                 160

Gly Phe Leu Ala Gln Glu Glu Leu Leu Pro Lys Arg Val Ile Asn Leu
                165                 170                 175

Tyr Gln Met Thr Pro Glu Met Trp Glu Glu Arg Ile Thr Ala Trp Tyr
            180                 185                 190

Ala Glu His Arg Gly Arg Ala Arg Asp Glu Ala Glu Met Glu Tyr Leu
        195                 200                 205

Lys Ile Ala Gln Asp Leu Glu Met Tyr Gly Val Asn Tyr Phe Ala Ile
    210                 215                 220

Arg Asn Lys Lys Gly Thr Glu Leu Leu Leu Gly Val Asp Ala Leu Gly
225                 230                 235                 240

Leu His Ile Tyr Asp Pro Glu Asn Arg Leu Thr Pro Lys Ile Ser Phe
                245                 250                 255

Pro Trp Lys Asn Glu Ile Arg Asn Ile Ser Tyr Ser Asp Lys Glu Phe
            260                 265                 270

Thr Ile Lys Pro Leu Asp Lys Lys Ile Asp Val Phe Lys Phe Asn Ser
        275                 280                 285

Ser Lys Leu Arg Val Asn Lys Leu Ile Leu Gln Leu Cys Ile Gly Asn
    290                 295                 300

His Asp Leu Phe Met Arg Arg Arg Lys Ala Asp Ser Leu Glu Val Gln
305                 310                 315                 320

Gln Met Lys Ala Gln Ala Arg Glu Glu Lys Ala Arg Lys Gln Met Lys
                325                 330                 335

Glu Glu Ala Thr Met Ala Asn Glu Ala Leu Met Arg Ser Glu Glu Thr
            340                 345                 350

Ala Asp Leu Leu Ala Glu Lys Ala Gln Ile Thr Glu Glu Glu Ala Lys
        355                 360                 365

Leu Leu Ala Gln Lys Ala Ala Glu Ala Glu Gln Glu Met Gln Arg Ile
    370                 375                 380

Lys Ala Thr Ala Ile Arg Thr Glu Glu Glu Lys Arg Leu Met Glu Gln
385                 390                 395                 400

Lys Val Leu Glu Ala Glu Val Leu Ala Leu Lys Met Ala Glu Glu Ser
                405                 410                 415

Glu Arg Arg Ala Lys Glu Ala Asp Gln Leu Lys Gln Asp Leu Gln Glu
            420                 425                 430

Ala Arg Glu Ala Glu Arg Arg Ala Lys Gln Lys Leu Leu Glu Ile Ala
```

```
        435                 440                 445

Thr Lys Pro Thr Tyr Pro Pro Met Asn Pro Ile Pro Ala Pro Leu Pro
    450                 455                 460

Pro Asp Ile Pro Ser Phe Asn Leu Ile Gly Asp Ser Leu Ser Phe Asp
465                 470                 475                 480

Phe Lys Asp Thr Asp Met Lys Arg Leu Ser Met Glu Ile Glu Lys Glu
                485                 490                 495

Lys Val Glu Tyr Met Glu Lys Ser Lys His Leu Gln Glu Gln Leu Asn
            500                 505                 510

Glu Leu Lys Thr Glu Ile Glu Ala Leu Lys Leu Lys Glu Arg Glu Thr
        515                 520                 525

Ala Leu Asp Ile Leu His Asn Glu Asn Ser Asp Arg Gly Gly Ser Ser
    530                 535                 540

Lys His Asn Thr Ile Lys Lys Leu Thr Leu Gln Ser Ala Lys Ser Arg
545                 550                 555                 560

Val Ala Phe Phe Glu Glu Leu
                565
```

<210> 65
<211> 134
<212> PRT
<213> Homo sapiens

<400> 65

```
Met Arg Glu Arg Phe Asp Arg Phe Leu His Glu Lys Asn Cys Met Thr
  1               5                  10                  15

Asp Leu Leu Ala Lys Leu Glu Ala Lys Thr Gly Val Asn Arg Ser Phe
             20                  25                  30

Ile Ala Leu Gly Val Ile Gly Leu Val Ala Leu Tyr Leu Val Phe Gly
         35                  40                  45

Tyr Gly Ala Ser Leu Leu Cys Asn Leu Ile Gly Phe Gly Tyr Pro Ala
     50                  55                  60

Tyr Ile Ser Ile Lys Ala Ile Glu Ser Pro Asn Lys Glu Asp Asp Thr
 65                  70                  75                  80

Gln Trp Leu Thr Tyr Trp Val Val Tyr Gly Val Phe Ser Ile Ala Glu
                 85                  90                  95

Phe Phe Ser Asp Ile Phe Leu Ser Trp Phe Pro Phe Tyr Tyr Met Leu
            100                 105                 110

Lys Gln Ile Tyr Leu Glu Pro Pro Cys Ala Arg Phe Cys Ser Thr Ser
        115                 120                 125

Gly Arg Tyr Phe Gly Glu
    130
```

<210> 66
<211> 1278
<212> PRT
<213> Homo sapiens

<400> 66

```
Met Asp Leu Glu Gly Asp Arg Asn Gly Gly Ala Lys Lys Lys Asn Phe
  1               5                  10                  15

Phe Lys Leu Asn Asn Lys Ser Glu Lys Asp Lys Lys Glu Lys Lys Pro
             20                  25                  30

Thr Val Ser Val Phe Ser Met Phe Arg Tyr Ser Asn Trp Leu Asp Lys
         35                  40                  45

Leu Tyr Met Val Val Gly Thr Leu Ala Ala Ile Ile His Gly Ala Gly
     50                  55                  60

Leu Pro Leu Met Met Leu Val Phe Gly Glu Met Thr Asp Ile Phe Ala
 65                  70                  75                  80

Asn Ala Gly Asn Leu Glu Asp Leu Met Ser Asn Ile Thr Asn Arg Ser
                 85                  90                  95

Asp Ile Asn Asp Thr Gly Phe Phe Met Asn Leu Glu Glu Asp Met Thr
            100                 105                 110

Arg Tyr Ala Tyr Tyr Tyr Ser Gly Ile Gly Ala Gly Val Leu Val Ala
        115                 120                 125

Ala Tyr Ile Gln Val Ser Phe Trp Cys Leu Ala Ala Gly Arg Gln Ile
    130                 135                 140

His Lys Ile Arg Lys Gln Phe Phe His Ala Ile Met Arg Gln Glu Ile
145                 150                 155                 160

Gly Trp Phe Asp Val His Asp Val Gly Glu Leu Asn Thr Arg Leu Thr
                165                 170                 175

Asp Asp Val Ser Lys Ile Asn Glu Val Ile Gly Asp Lys Ile Gly Met
            180                 185                 190

Phe Phe Gln Ser Met Ala Thr Phe Phe Thr Gly Phe Ile Val Gly Phe
        195                 200                 205

Thr Arg Gly Trp Lys Leu Thr Leu Val Ile Leu Ala Ile Ser Pro Val
    210                 215                 220

Leu Gly Leu Ser Ala Ala Val Trp Ala Lys Ile Leu Ser Ser Phe Thr
225                 230                 235                 240

Asp Lys Glu Leu Leu Ala Tyr Ala Lys Ala Gly Ala Val Ala Glu Glu
                245                 250                 255

Val Leu Ala Ala Ile Arg Thr Val Ile Ala Phe Gly Gly Gln Lys Lys
            260                 265                 270

Glu Leu Glu Arg Tyr Asn Lys Asn Leu Glu Glu Ala Lys Arg Ile Gly
        275                 280                 285
```

Ile Lys Lys Ala Ile Thr Ala Asn Ile Ser Ile Gly Ala Ala Phe Leu
290 295 300

Leu Ile Tyr Ala Ser Tyr Ala Leu Ala Phe Trp Tyr Gly Thr Thr Leu
305 310 315 320

Val Leu Ser Gly Glu Tyr Ser Ile Gly Gln Val Leu Thr Val Phe Phe
325 330 335

Ser Val Leu Ile Gly Ala Phe Ser Val Gly Gln Ala Ser Pro Ser Ile
340 345 350

Glu Ala Phe Ala Asn Ala Arg Gly Ala Ala Tyr Glu Ile Phe Lys Ile
355 360 365

Ile Asp Asn Lys Pro Ser Ile Asp Ser Tyr Ser Lys Ser Gly His Lys
370 375 380

Pro Asp Asn Ile Lys Gly Asn Leu Glu Phe Arg Asn Val His Phe Ser
385 390 395 400

Tyr Pro Ser Arg Lys Glu Val Lys Ile Leu Lys Gly Leu Asn Leu Lys
405 410 415

Val Gln Ser Gly Gln Thr Val Ala Leu Val Gly Asn Ser Gly Cys Gly
420 425 430

Lys Ser Thr Thr Val Gln Leu Met Gln Arg Leu Tyr Asp Pro Thr Glu
435 440 445

Gly Met Val Ser Val Asp Gly Gln Asp Ile Arg Thr Ile Asn Val Arg
450 455 460

Phe Leu Arg Glu Ile Ile Gly Val Val Ser Gln Glu Pro Val Leu Phe
465 470 475 480

Ala Thr Thr Ile Ala Glu Asn Ile Arg Tyr Gly Arg Glu Asn Val Thr
485 490 495

Met Asp Glu Ile Glu Lys Ala Val Lys Glu Ala Asn Ala Tyr Asp Phe
500 505 510

Ile Met Lys Leu Pro His Lys Phe Asp Thr Leu Val Gly Glu Arg Gly
515 520 525

Ala Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg Ala
530 535 540

Leu Val Arg Asn Pro Lys Ile Leu Leu Leu Asp Glu Ala Thr Ser Ala
545 550 555 560

Leu Asp Thr Glu Ser Glu Ala Val Val Gln Val Ala Leu Asp Lys Ala
565 570 575

Arg Lys Gly Arg Thr Thr Ile Val Ile Ala His Arg Leu Ser Thr Val
580 585 590

Arg Asn Ala Asp Val Ile Ala Gly Phe Asp Asp Gly Val Ile Val Glu
595 600 605

Lys Gly Asn His Asp Glu Leu Met Lys Glu Lys Gly Ile Tyr Phe Lys
610 615 620

Leu Val Thr Met Gln Thr Ala Gly Asn Glu Val Glu Leu Glu Asn Ala
625 630 635 640

Ala Asp Glu Ser Lys Ser Glu Ile Asp Ala Leu Glu Met Ser Ser Asn
645 650 655

Asp Ser Arg Ser Ser Leu Ile Arg Lys Arg Ser Thr Arg Arg Ser Val
660 665 670

Arg Gly Ser Gln Ala Gln Asp Arg Lys Leu Ser Thr Lys Glu Ala Leu
675 680 685

Asp Glu Ser Ile Pro Pro Val Ser Phe Trp Arg Ile Met Lys Leu Asn
690 695 700

Leu Thr Glu Trp Pro Tyr Phe Val Val Gly Val Phe Cys Ala Ile Ile
705 710 715 720

Asn Gly Gly Leu Gln Pro Ala Phe Ala Ile Ile Phe Ser Lys Ile Ile
725 730 735

Gly Val Phe Thr Arg Ile Asp Asp Pro Glu Thr Lys Arg Gln Asn Ser
740 745 750

Asn Leu Phe Ser Leu Leu Phe Leu Ala Leu Gly Ile Ile Ser Phe Ile
755 760 765

Thr Phe Phe Leu Gln Gly Phe Thr Phe Gly Lys Ala Gly Glu Ile Leu
770 775 780

Thr Lys Arg Leu Arg Tyr Met Val Phe Arg Ser Met Leu Arg Gln Asp
785 790 795 800

Val Ser Trp Phe Asp Asp Pro Lys Asn Thr Thr Gly Ala Leu Thr Thr
805 810 815

Arg Leu Ala Asn Asp Ala Ala Gln Val Lys Gly Ala Ile Gly Ser Arg
820 825 830

Leu Ala Val Ile Thr Gln Asn Ile Ala Asn Leu Gly Thr Gly Ile Ile
835 840 845

Ile Ser Phe Ile Tyr Gly Trp Gln Leu Thr Leu Leu Leu Leu Ala Ile
850 855 860

Val Pro Ile Ile Ala Ile Ala Gly Val Val Glu Met Lys Met Leu Ser
865 870 875 880

Gly Gln Ala Leu Lys Asp Lys Lys Glu Leu Glu Gly Ala Gly Lys Ile
885 890 895

Ala Thr Glu Ala Ile Glu Asn Phe Arg Thr Val Val Ser Leu Thr Gln
900 905 910

Glu Gln Lys Phe Glu His Met Tyr Ala Gln Ser Leu Gln Val Pro Tyr
915 920 925

Arg Asn Ser Leu Arg Lys Ala His Ile Phe Gly Ile Thr Phe Ser Phe

```
    930                 935                 940

Thr Gln Ala Met Met Tyr Phe Ser Tyr Ala Gly Cys Phe Arg Phe Gly
945                 950                 955                 960

Ala Tyr Leu Val Ala His Lys Leu Met Ser Phe Glu Asp Val Leu Leu
                965                 970                 975

Val Phe Ser Ala Val Val Phe Gly Ala Met Ala Val Gly Gln Val Ser
            980                 985                 990

Ser Phe Ala Pro Asp Tyr Ala Lys Ala Lys Ile Ser Ala Ala His Ile
        995                1000                1005

Ile Met Ile Ile Glu Lys Thr Pro Leu Ile Asp Ser Tyr Ser Thr Glu
   1010                1015                1020

Gly Leu Met Pro Asn Thr Leu Glu Gly Asn Val Thr Phe Gly Glu Val
1025                1030                1035                1040

Val Phe Asn Tyr Pro Thr Arg Pro Asp Ile Pro Val Leu Gln Gly Leu
                1045                1050                1055

Ser Leu Glu Val Lys Lys Gly Gln Thr Leu Ala Leu Val Gly Ser Ser
            1060                1065                1070

Gly Cys Gly Lys Ser Thr Val Val Gln Leu Leu Glu Arg Phe Tyr Asp
        1075                1080                1085

Pro Leu Ala Gly Lys Val Leu Leu Asp Gly Lys Glu Ile Lys Arg Leu
   1090                1095                1100

Asn Val Gln Trp Leu Arg Ala His Leu Gly Ile Val Ser Gln Glu Pro
1105                1110                1115                1120

Ile Leu Phe Asp Cys Ser Ile Ala Glu Asn Ile Ala Tyr Gly Asp Asn
                1125                1130                1135

Ser Arg Val Val Ser Gln Glu Glu Ile Val Arg Ala Ala Lys Glu Ala
            1140                1145                1150

Asn Ile His Ala Phe Ile Glu Ser Leu Pro Asn Lys Tyr Ser Thr Lys
        1155                1160                1165

Val Gly Asp Lys Gly Thr Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile
   1170                1175                1180

Ala Ile Ala Arg Ala Leu Val Arg Gln Pro His Ile Leu Leu Leu Asp
1185                1190                1195                1200

Glu Ala Thr Ser Ala Leu Asp Thr Glu Ser Glu Lys Val Val Gln Glu
                1205                1210                1215

Ala Leu Asp Lys Ala Arg Glu Gly Arg Thr Cys Ile Val Ile Ala His
            1220                1225                1230

Arg Leu Ser Thr Ile Gln Asn Ala Asp Leu Ile Val Val Phe Gln Asn
        1235                1240                1245

Gly Arg Val Lys Glu His Gly Thr His Gln Gln Leu Leu Ala Gln Lys
   1250                1255                1260
```

```
Gly Ile Tyr Phe Ser Met Val Ser Val Gln Ala Gly Thr Ile
1265                1270                1275


<210> 67
<211> 579
<212> PRT
<213> Homo sapiens

<400> 67
Met Asp Leu Glu Gly Asp Arg Asn Gly Gly Ala Lys Lys Lys Asn Phe
  1               5                  10                  15

Phe Lys Leu Asn Asn Lys Ser Glu Lys Asp Lys Lys Glu Lys Lys Pro
             20                  25                  30

Thr Val Ser Val Phe Ser Met Phe Arg Tyr Ser Asn Trp Leu Asp Lys
         35                  40                  45

Leu Tyr Met Val Val Gly Thr Leu Ala Ala Ile Ile His Gly Ala Gly
     50                  55                  60

Leu Pro Leu Met Met Leu Val Phe Gly Glu Met Thr Asp Ile Phe Ala
 65                  70                  75                  80

Asn Ala Gly Asn Leu Glu Asp Leu Met Ser Asn Ile Thr Asn Arg Ser
                 85                  90                  95

Asp Ile Asn Asp Thr Gly Phe Phe Met Asn Leu Glu Glu Asp Met Thr
            100                 105                 110

Arg Tyr Ala Tyr Tyr Tyr Ser Gly Ile Gly Ala Gly Val Leu Val Ala
        115                 120                 125

Ala Tyr Ile Gln Val Ser Phe Trp Cys Leu Ala Ala Gly Arg Gln Ile
    130                 135                 140

His Lys Ile Arg Lys Gln Phe Phe His Ala Ile Met Arg Gln Glu Ile
145                 150                 155                 160

Gly Trp Phe Asp Val His Asp Val Gly Glu Leu Asn Thr Arg Leu Thr
                165                 170                 175

Asp Asp Val Ser Lys Ile Asn Glu Gly Ile Gly Asp Lys Ile Gly Met
            180                 185                 190

Phe Phe Gln Ser Met Ala Thr Phe Phe Thr Gly Phe Ile Val Gly Phe
        195                 200                 205

Thr Arg Gly Trp Lys Leu Thr Leu Val Ile Leu Ala Ile Ser Pro Val
    210                 215                 220

Leu Gly Leu Ser Ala Ala Val Trp Ala Lys Ile Leu Ser Ser Phe Thr
225                 230                 235                 240

Asp Lys Glu Leu Leu Ala Tyr Ala Lys Ala Gly Ala Val Ala Glu Glu
                245                 250                 255

Val Leu Ala Ala Ile Arg Thr Val Ile Ala Phe Gly Gly Gln Lys Lys
```

260 265 270

Glu Leu Glu Arg Tyr Asn Lys Asn Leu Glu Glu Ala Lys Arg Ile Gly
275 280 285

Ile Lys Lys Ala Ile Thr Ala Asn Ile Ser Ile Gly Ala Ala Phe Leu
290 295 300

Leu Ile Tyr Ala Ser Tyr Ala Leu Ala Phe Trp Tyr Gly Thr Thr Leu
305 310 315 320

Val Leu Ser Gly Glu Tyr Ser Ile Gly Gln Val Leu Thr Val Phe Phe
325 330 335

Ser Val Leu Ile Gly Ala Phe Ser Val Gly Gln Ala Ser Pro Ser Ile
340 345 350

Glu Ala Phe Ala Asn Ala Arg Gly Ala Ala Tyr Glu Ile Phe Lys Ile
355 360 365

Ile Asp Asn Lys Pro Ser Ile Asp Ser Tyr Ser Lys Ser Gly His Lys
370 375 380

Pro Asp Asn Ile Lys Gly Asn Leu Glu Phe Arg Asn Val His Phe Ser
385 390 395 400

Tyr Pro Ser Arg Lys Glu Val Lys Ile Leu Lys Gly Leu Asn Leu Lys
405 410 415

Val Gln Ser Gly Gln Thr Val Ala Leu Val Gly Asn Ser Gly Cys Gly
420 425 430

Lys Ser Thr Thr Val Gln Leu Met Gln Arg Leu Tyr Asp Pro Thr Glu
435 440 445

Gly Met Val Ser Val Asp Gly Gln Asp Ile Arg Thr Ile Asn Val Arg
450 455 460

Phe Leu Arg Glu Ile Ile Gly Val Val Ser Gln Glu Pro Val Leu Phe
465 470 475 480

Ala Thr Thr Ile Ala Glu Asn Ile Arg Tyr Gly Arg Glu Asn Val Thr
485 490 495

Met Asp Glu Ile Glu Lys Ala Val Lys Glu Ala Asn Ala Tyr Asp Phe
500 505 510

Ile Met Lys Leu Pro His Lys Phe Asp Thr Leu Val Gly Glu Arg Gly
515 520 525

Ala Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg Ala
530 535 540

Leu Val Arg Asn Pro Lys Ile Leu Leu Leu Asp Glu Ala Thr Ser Ala
545 550 555 560

Leu Asp Thr Glu Ser Glu Ala Glu Val Gln Ala Ala Leu Asp Lys Val
565 570 575

Ser Arg Leu

<210> 68
<211> 218
<212> PRT
<213> Homo sapiens

<400> 68
Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
1 5 10 15

Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
20 25 30

Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
35 40 45

Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
50 55 60

Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
65 70 75 80

Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
85 90 95

Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
100 105 110

Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
115 120 125

Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
130 135 140

Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
145 150 155 160

Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
165 170 175

Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
180 185 190

Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Gly Gly Arg
195 200 205

Met Gly Lys Gly Ile Phe Thr Arg Leu Gln
210 215

<210> 69
<211> 307
<212> PRT
<213> Homo sapiens

<400> 69
Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
1 5 10 15

```
Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
             20                  25                  30

Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
         35                  40                  45

Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
     50                  55                  60

Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
 65                  70                  75                  80

Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
                 85                  90                  95

Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
            100                 105                 110

Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
        115                 120                 125

Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
    130                 135                 140

Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
145                 150                 155                 160

Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
                165                 170                 175

Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
            180                 185                 190

Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
        195                 200                 205

Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
    210                 215                 220

Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
225                 230                 235                 240

Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
                245                 250                 255

Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
            260                 265                 270

Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
        275                 280                 285

Leu Lys Ala Ser Gln Tyr Phe Leu Gln Ile Cys Thr Phe Asn Pro Ile
    290                 295                 300

Trp Gly Val
305
```

<210> 70

<211> 339
<212> PRT
<213> Homo sapiens

<400> 70
Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
1 5 10 15

Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
20 25 30

Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
35 40 45

Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
50 55 60

Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
65 70 75 80

Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
85 90 95

Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
100 105 110

Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
115 120 125

Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
130 135 140

Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
145 150 155 160

Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
165 170 175

Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
180 185 190

Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
195 200 205

Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
210 215 220

Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
225 230 235 240

Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
245 250 255

Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
260 265 270

Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
275 280 285

Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu Ser Lys Met Leu Val Ile
290 295 300

```
Asp Ala Ser Lys Arg Ile Ser Val Asp Glu Ala Leu Gln His Pro Tyr
305                 310                 315                 320

Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Arg Ser Cys Lys
                325                 330                 335

Leu Phe Ser
```

<210> 71
<211> 178
<212> PRT
<213> Homo sapiens

<400> 71

```
Ala Arg Ser Gly Phe Tyr Arg Gln Glu Val Thr Lys Thr Ala Trp Glu
  1               5                  10                  15

Val Arg Ala Val Tyr Arg Asp Leu Gln Pro Val Gly Ser Gly Ala Tyr
             20                  25                  30

Gly Ala Val Cys Ser Ala Val Asp Gly Arg Thr Gly Ala Lys Val Ala
         35                  40                  45

Ile Lys Lys Leu Tyr Arg Pro Phe Gln Ser Glu Leu Phe Ala Lys Arg
     50                  55                  60

Ala Tyr Arg Glu Leu Arg Leu Leu Lys His Met Arg His Glu Asn Val
 65                  70                  75                  80

Ile Gly Leu Leu Asp Val Phe Thr Pro Asp Glu Thr Leu Asp Asp Phe
                85                  90                  95

Thr Asp Phe Tyr Leu Val Met Pro Phe Met Gly Thr Asp Leu Gly Lys
            100                 105                 110

Leu Met Lys His Glu Lys Leu Gly Glu Asp Arg Ile Gln Phe Leu Val
        115                 120                 125

Tyr Gln Met Leu Lys Gly Leu Arg Tyr Ile His Ala Ala Gly Ile Ile
    130                 135                 140

His Arg Val Ser Pro Gly Gly Glu Ala Ala His Gln Pro Ser Pro Ser
145                 150                 155                 160

Ala Ile Pro Pro Pro Pro Arg Pro Thr Cys Glu Asp Val Met Gly Ser
                165                 170                 175

Gly Cys
```

<210> 72
<211> 648
<212> PRT
<213> Homo sapiens

<400> 72

```
Met Ser Pro Phe Leu Arg Ile Gly Leu Ser Asn Phe Asp Cys Gly Ser
  1               5                  10                  15

Cys Gln Ser Cys Gln Gly Glu Ala Val Asn Pro Tyr Cys Ala Val Leu
             20                  25                  30

Val Lys Glu Tyr Val Glu Ser Glu Asn Gly Gln Met Tyr Ile Gln Lys
         35                  40                  45

Lys Pro Thr Met Tyr Pro Pro Trp Asp Ser Thr Phe Asp Ala His Ile
     50                  55                  60

Asn Lys Gly Arg Val Met Gln Ile Ile Val Lys Gly Lys Asn Val Asp
 65                  70                  75                  80

Leu Ile Ser Glu Thr Thr Val Glu Leu Tyr Ser Leu Ala Glu Arg Cys
                 85                  90                  95

Arg Lys Asn Asn Gly Lys Thr Glu Ile Trp Leu Glu Leu Lys Pro Gln
            100                 105                 110

Gly Arg Met Leu Met Asn Ala Arg Tyr Phe Leu Glu Met Ser Asp Thr
        115                 120                 125

Lys Asp Met Asn Glu Phe Glu Thr Glu Gly Phe Phe Ala Leu His Gln
    130                 135                 140

Arg Arg Gly Ala Ile Lys Gln Ala Lys Val His His Val Lys Cys His
145                 150                 155                 160

Glu Phe Thr Ala Thr Phe Phe Pro Gln Pro Thr Phe Cys Ser Val Cys
                165                 170                 175

His Glu Phe Val Trp Gly Leu Asn Lys Gln Gly Tyr Gln Cys Arg Gln
            180                 185                 190

Cys Asn Ala Ala Ile His Lys Lys Cys Ile Asp Lys Val Ile Ala Lys
        195                 200                 205

Cys Thr Gly Ser Ala Ile Asn Ser Arg Glu Thr Met Phe His Lys Glu
    210                 215                 220

Arg Phe Lys Ile Asp Met Pro His Arg Phe Lys Val Tyr Asn Tyr Lys
225                 230                 235                 240

Ser Pro Thr Phe Cys Glu His Cys Gly Thr Leu Leu Trp Gly Leu Ala
                245                 250                 255

Arg Gln Gly Leu Lys Cys Asp Ala Cys Gly Met Asn Val His His Arg
            260                 265                 270

Cys Gln Thr Lys Val Ala Asn Leu Cys Gly Ile Asn Gln Lys Leu Met
        275                 280                 285

Ala Glu Ala Leu Ala Met Ile Glu Ser Thr Gln Gln Ala Arg Cys Leu
    290                 295                 300

Arg Asp Thr Glu Gln Ile Phe Arg Glu Gly Pro Val Glu Ile Gly Leu
305                 310                 315                 320
```

Pro Cys Ser Ile Lys Asn Glu Ala Arg Pro Pro Cys Leu Pro Thr Pro
325 330 335

Gly Lys Arg Glu Pro Gln Gly Ile Ser Trp Glu Ser Pro Leu Asp Glu
340 345 350

Val Asp Lys Met Cys His Leu Pro Glu Pro Glu Leu Asn Lys Glu Arg
355 360 365

Pro Ser Leu Gln Ile Lys Leu Lys Ile Glu Asp Phe Ile Leu His Lys
370 375 380

Met Leu Gly Lys Gly Ser Phe Gly Lys Val Phe Leu Ala Glu Phe Lys
385 390 395 400

Lys Thr Asn Gln Phe Phe Ala Ile Lys Ala Leu Lys Lys Asp Val Val
405 410 415

Leu Met Asp Asp Asp Val Glu Cys Thr Met Val Glu Lys Arg Val Leu
420 425 430

Ser Leu Ala Trp Glu His Pro Phe Leu Thr His Met Phe Cys Thr Phe
435 440 445

Gln Thr Lys Glu Asn Leu Phe Phe Val Met Glu Tyr Leu Asn Gly Gly
450 455 460

Asp Leu Met Tyr His Ile Gln Ser Cys His Lys Phe Asp Leu Ser Arg
465 470 475 480

Ala Thr Phe Tyr Ala Ala Glu Ile Ile Leu Gly Leu Gln Phe Leu His
485 490 495

Ser Lys Gly Ile Val Tyr Arg Asp Leu Lys Leu Asp Asn Ile Leu Leu
500 505 510

Asp Lys Asp Gly His Ile Lys Ile Ala Asp Phe Gly Met Cys Lys Glu
515 520 525

Asn Met Leu Gly Asp Ala Lys Thr Asn Thr Phe Cys Gly Thr Pro Asp
530 535 540

Tyr Ile Ala Pro Glu Ile Leu Leu Gly Gln Lys Tyr Asn His Ser Val
545 550 555 560

Asp Trp Trp Ser Phe Gly Val Leu Leu Tyr Glu Met Leu Ile Gly Gln
565 570 575

Ser Pro Phe His Gly Gln Asp Glu Glu Glu Leu Phe His Ser Ile Arg
580 585 590

Met Asp Asn Pro Phe Tyr Pro Arg Trp Leu Glu Lys Glu Ala Lys Asp
595 600 605

Leu Leu Val Lys Val Arg Ser Glu Ala Lys Ser Val Phe Ile Arg Arg
610 615 620

Ala Leu Gly Leu Leu Val Ser Phe Leu Phe Leu Leu Val Ser Asn Leu
625 630 635 640

His Val Ala Asn Asn Asp Tyr Tyr

645

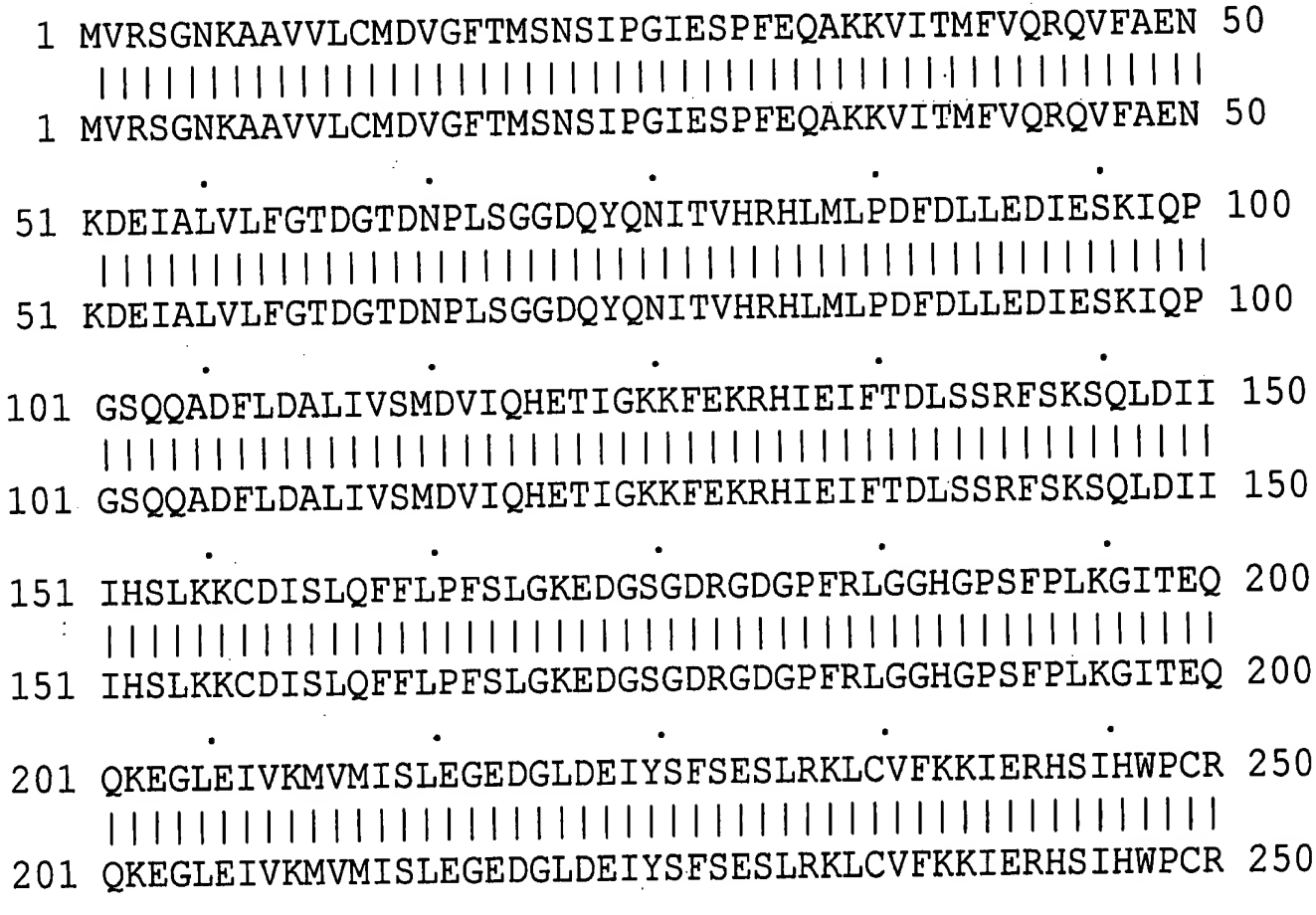

Fig. 1

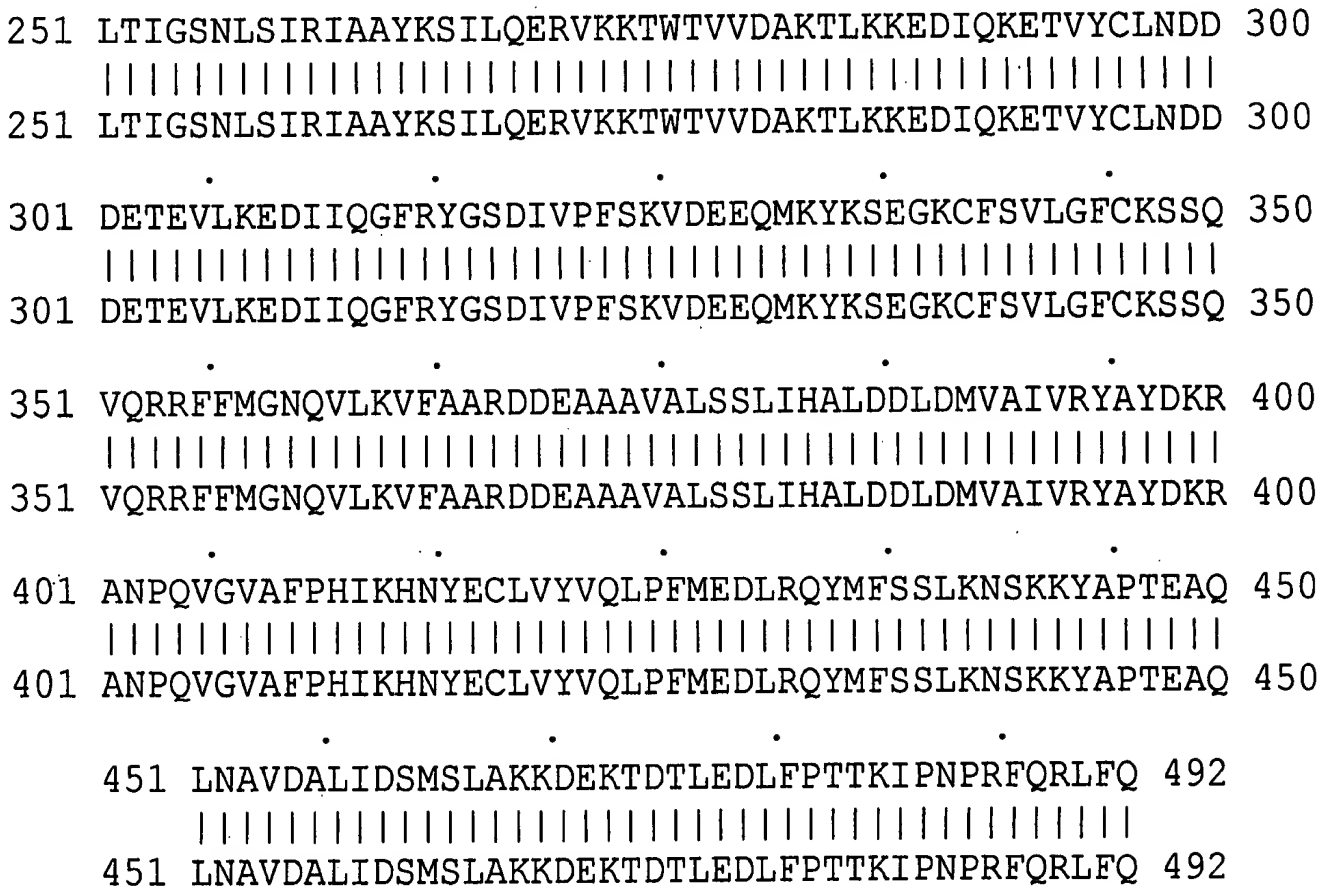

Fig. 1(Cont.)

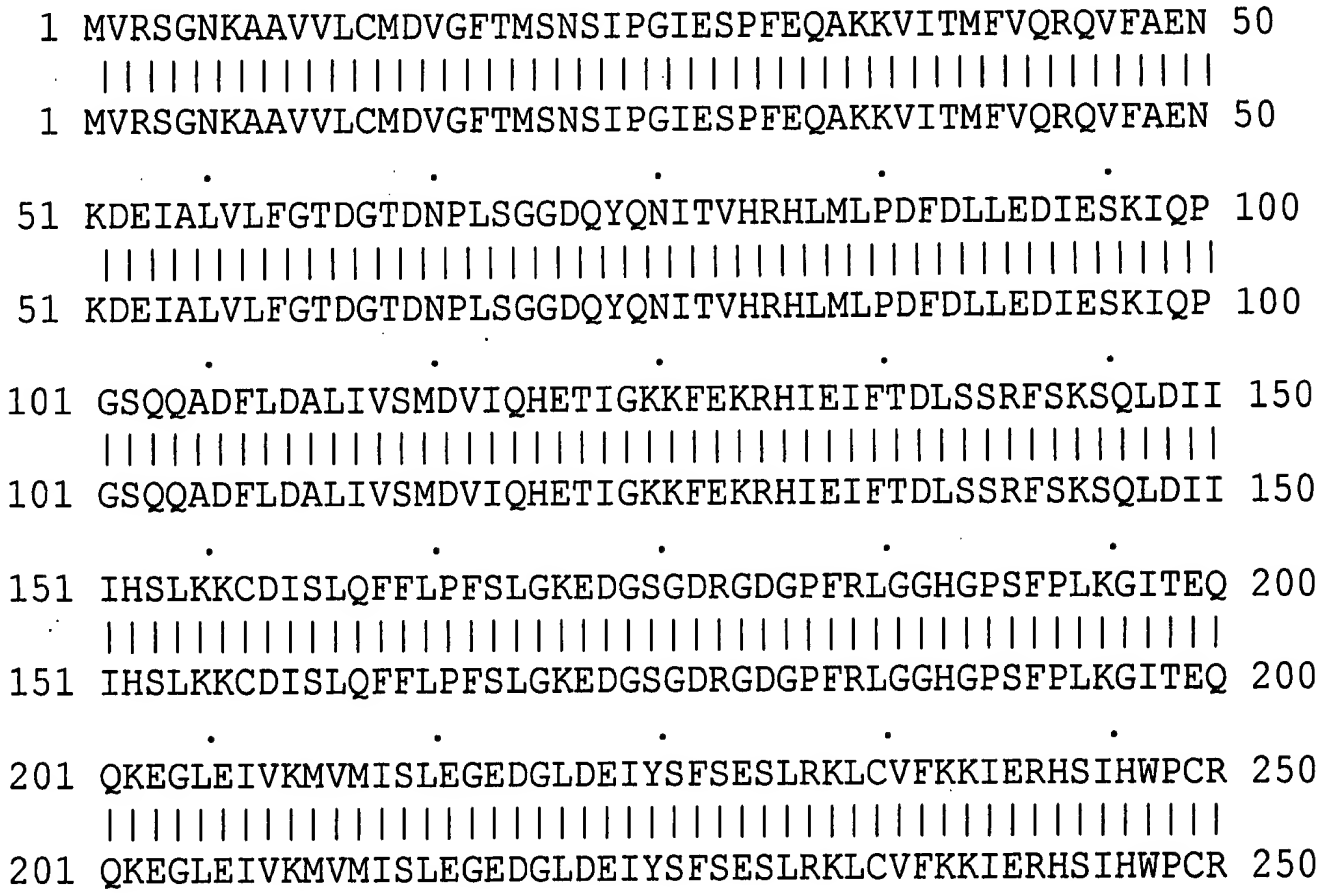

Fig. 2.

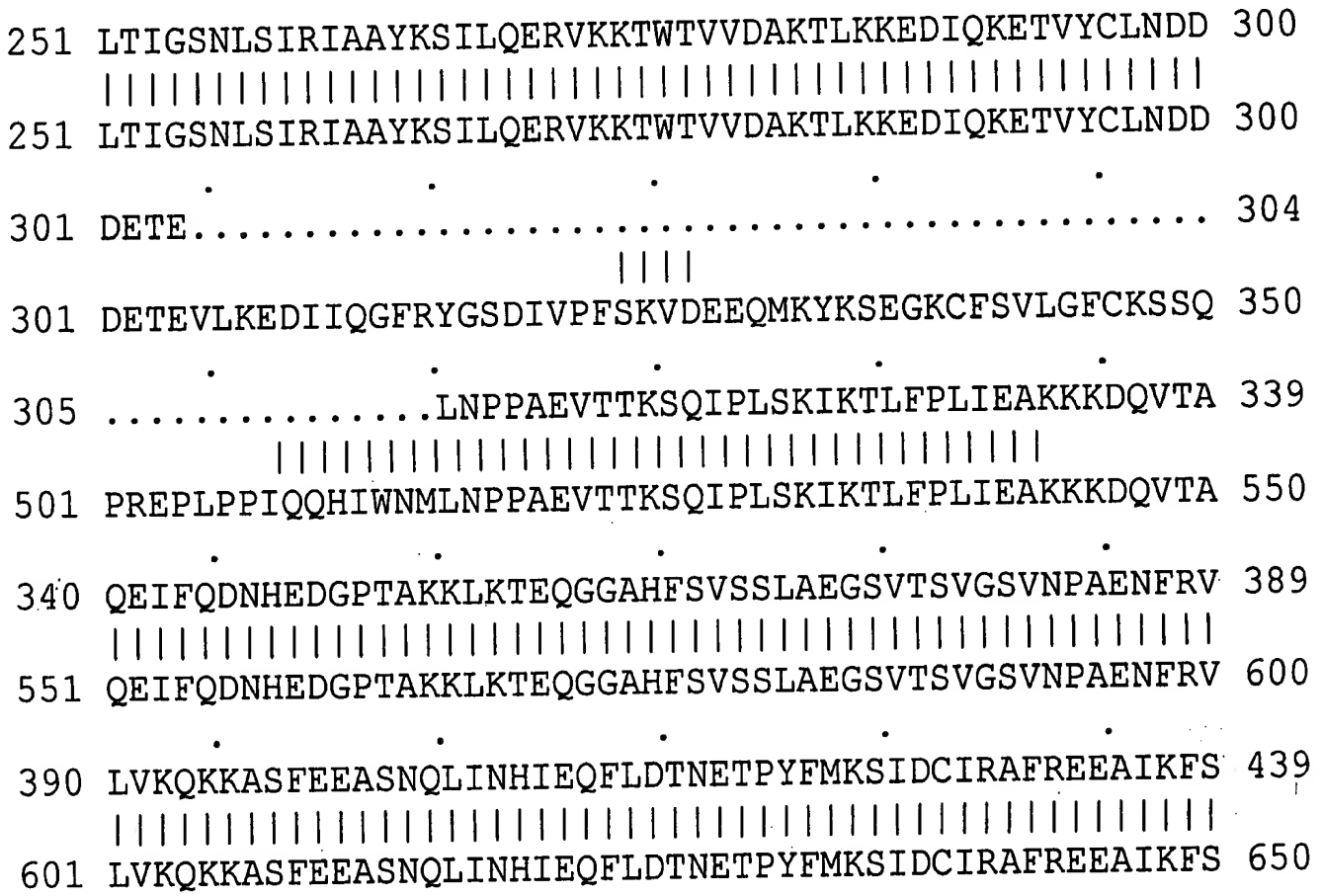
251 LTIGSNLSIRIAAYKSILQERVKKTWTVVDAKTLKKEDIQKETVYCLNDD 300
251 LTIGSNLSIRIAAYKSILQERVKKTWTVVDAKTLKKEDIQKETVYCLNDD 300
301 DETE 304
301 DETEVLKEDIIQGFRYGSDIVPFSKVDEEQMKYKSEGKCFSVLGFCKSSQ 350
305 LNPPAEVTTKSQIPLSKIKTLFPLIEAKKKDQVTA 339
501 PREPLPPIQQHIWNMLNPPAEVTTKSQIPLSKIKTLFPLIEAKKKDQVTA 550
340 QEIFQDNHEDGPTAKKLKTEQGGAHFSVSSLAEGSVTSVGSVNPAENFRV 389
551 QEIFQDNHEDGPTAKKLKTEQGGAHFSVSSLAEGSVTSVGSVNPAENFRV 600
390 LVKQKKASFEEASNQLINHIEQFLDTNETPYFMKSIDCIRAFREEAIKFS 439
601 LVKQKKASFEEASNQLINHIEQFLDTNETPYFMKSIDCIRAFREEAIKFS 650

Fig. 2(Cont.)

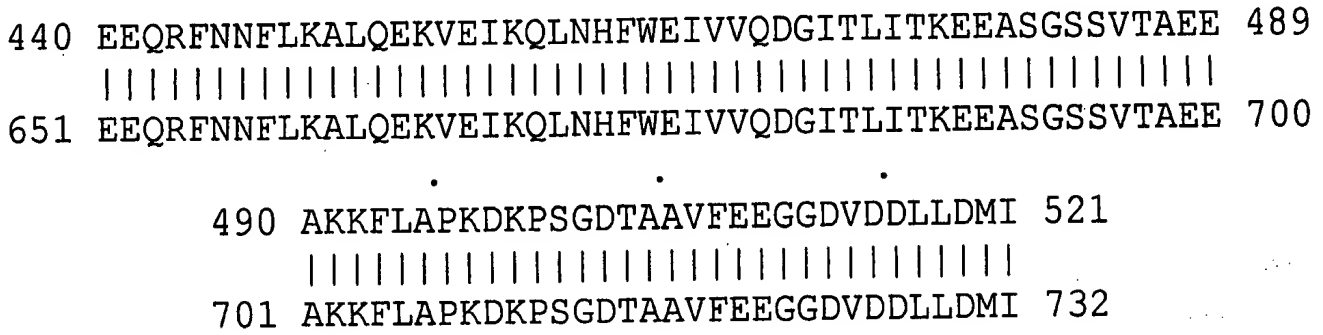

Fig. 2(Cont.)

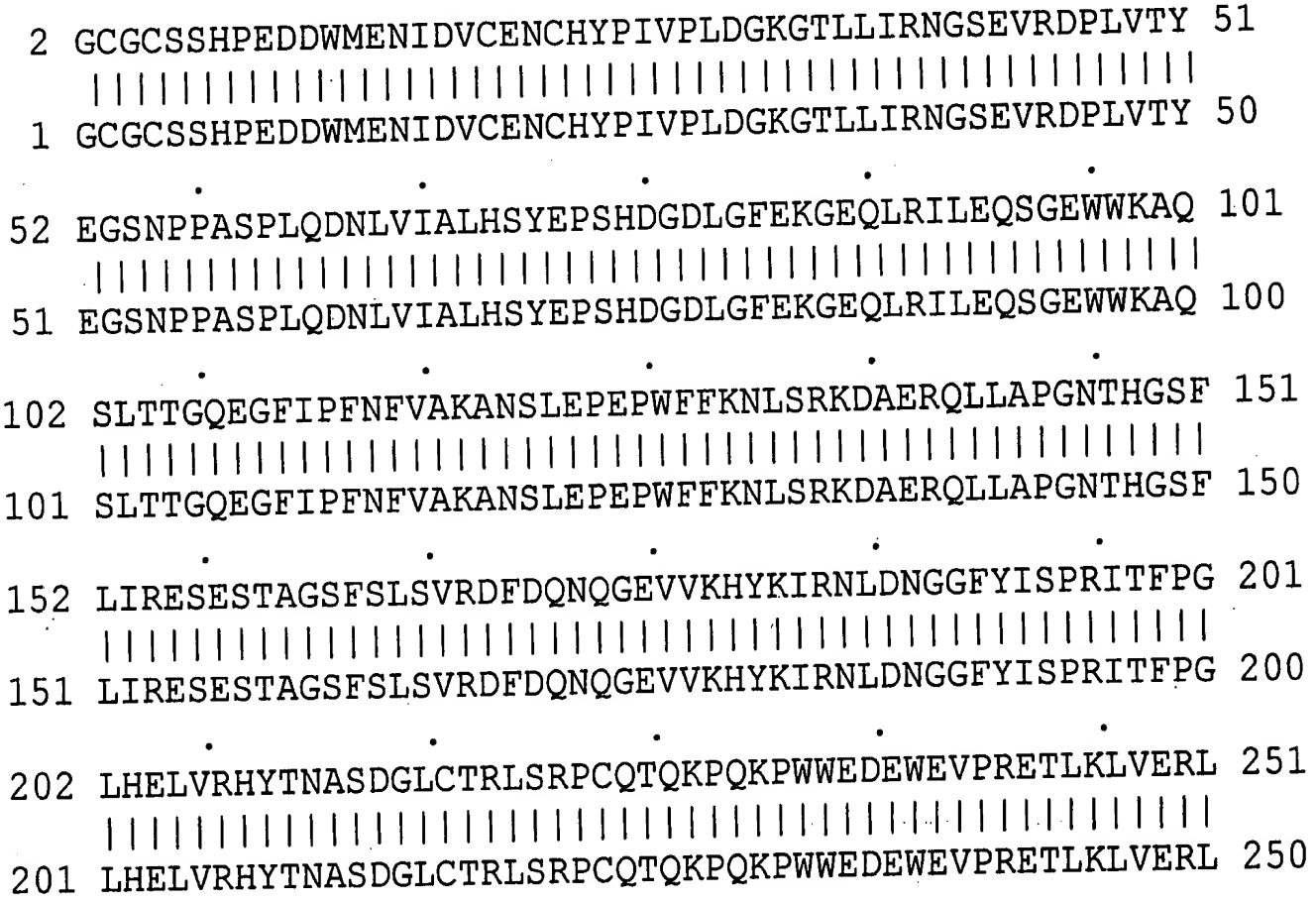
2 GCGCSSHPEDDWMENIDVCENCHYPIVPLDGKGTLLIRNGSEVRDPLVTY 51
1 GCGCSSHPEDDWMENIDVCENCHYPIVPLDGKGTLLIRNGSEVRDPLVTY 50
52 EGSNPPASPLQDNLVIALHSYEPSHDGDLGFEKGEQLRILEQSGEWWKAQ 101
51 EGSNPPASPLQDNLVIALHSYEPSHDGDLGFEKGEQLRILEQSGEWWKAQ 100
102 SLTTGQEGFIPFNFVAKANSLEPEPWFFKNLSRKDAERQLLAPGNTHGSF 151
101 SLTTGQEGFIPFNFVAKANSLEPEPWFFKNLSRKDAERQLLAPGNTHGSF 150
152 LIRESESTAGSFSLSVRDFDQNQGEVVKHYKIRNLDNGGFYISPRITFPG 201
151 LIRESESTAGSFSLSVRDFDQNQGEVVKHYKIRNLDNGGFYISPRITFPG 200
202 LHELVRHYTNASDGLCTRLSRPCQTQKPQKPWWEDEWEVPRETLKLVERL 251
201 LHELVRHYTNASDGLCTRLSRPCQTQKPQKPWWEDEWEVPRETLKLVERL 250

Fig. 3

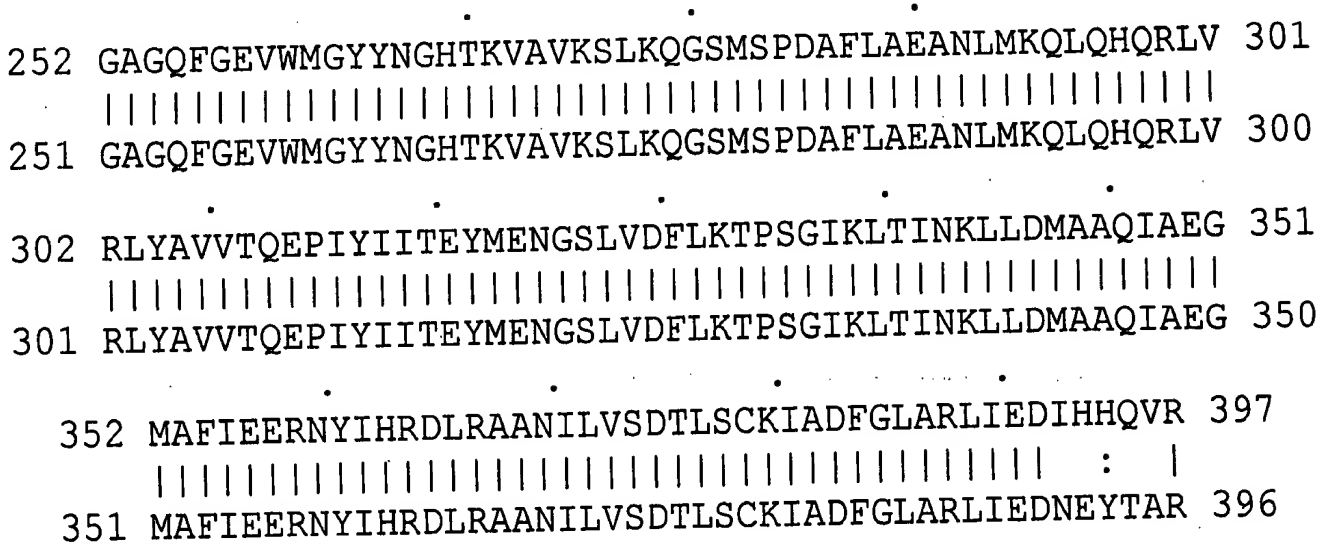

Fig. 3(Cont.)

```
302 TLKLVERLGAGQFGEVWMGYYNGHTKVAVKSLKQGSMSPDAFLAEANLMK 351
    ||||||||||||||||||||||||||||||||||||||||||||||||||
243 TLKLVERLGAGQFGEVWMGYYNGHTKVAVKSLKQGSMSPDAFLAEANLMK 292

352 QLQHQRLVRLYAVVTQEPIYIITEYMENGSLVDFLKTPSGIKLTINKLLD 401
    ||||||||||||||||||||||||||||||||||||||||||||||||||
293 QLQHQRLVRLYAVVTQEPIYIITEYMENGSLVDFLKTPSGIKLTINKLLD 342

402 MAAQIAEGMAFIEERNYIHRDLRAANILVSDTLSCKIADFGLARLIEDNE 451
    ||||||||||||||||||||||||||||||||||||||||||||||||||
343 MAAQIAEGMAFIEERNYIHRDLRAANILVSDTLSCKIADFGLARLIEDNE 392

452 YTAREGAKFPIKWTAPEAINYGTFTIKSDVWSFGILLTEIVTHGRIPYPG 501
    ||||||||||||||||||||||||||||||||||||||||||||||||||
393 YTAREGAKFPIKWTAPEAINYGTFTIKSDVWSFGILLTEIVTHGRIPYPG 442

502 MTNPEVIQNLERGYRMVRPDNCPEELYQLMRLCWKERPEDRPTFDYLRSV 551
    ||||||||||||||||||||||||||||||||||||||||||||||||||
443 MTNPEVIQNLERGYRMVRPDNCPEELYQLMRLCWKERPEDRPTFDYLRSV 492

552 LEDFFTATEGQYQPQP 567
    ||||||||||||||||
493 LEDFFTATEGQYQPQP 508
```

Fig. 4 (Cont.)

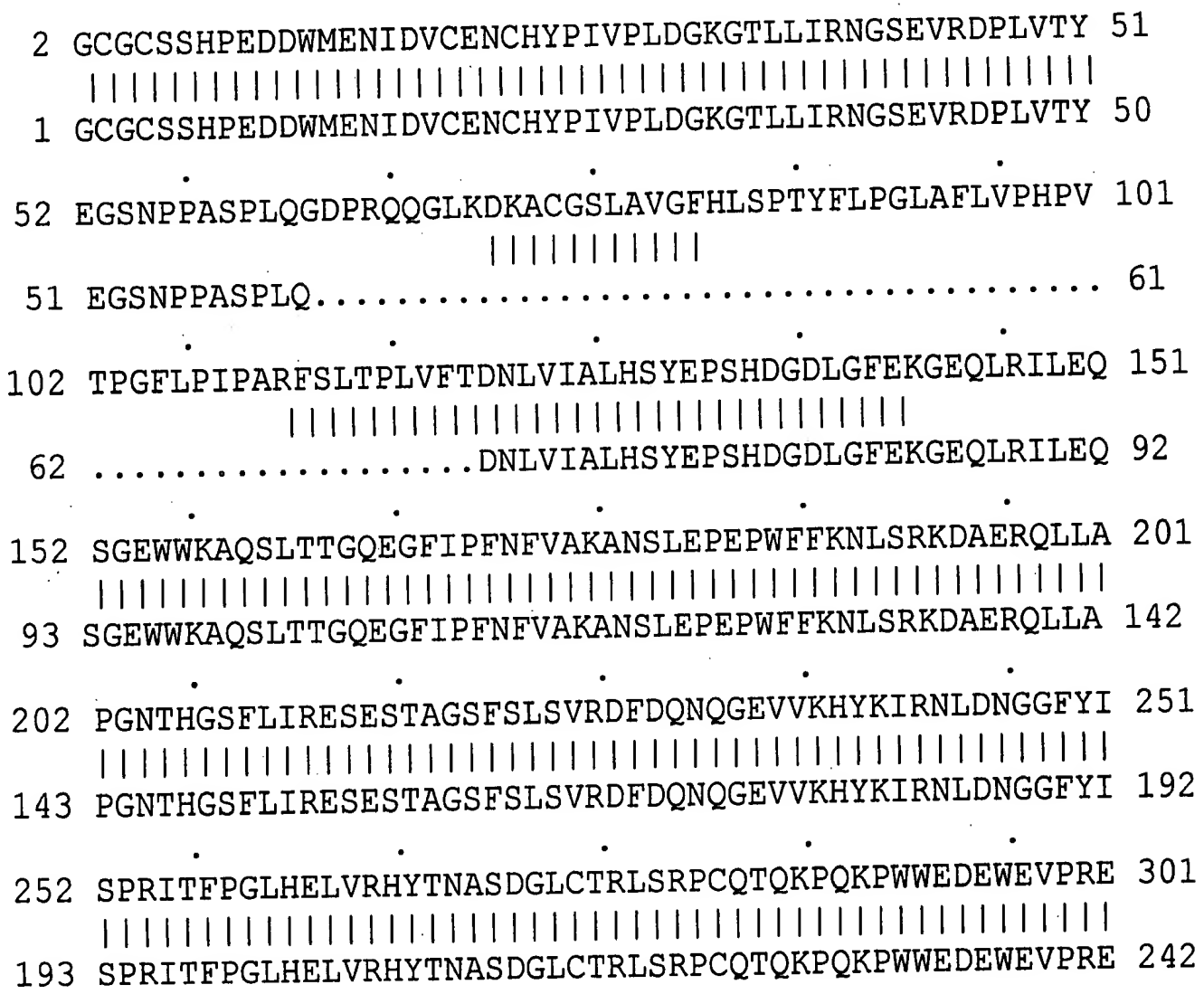

Fig. 4

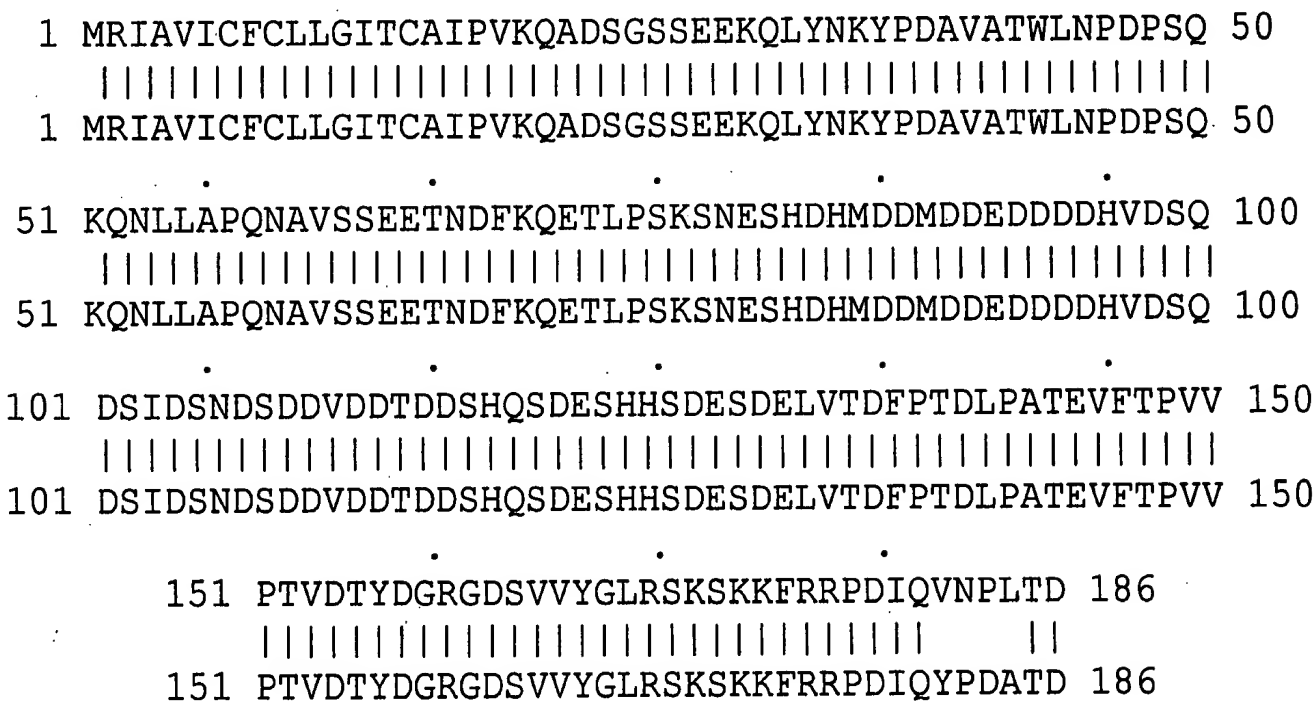

Fig. 5

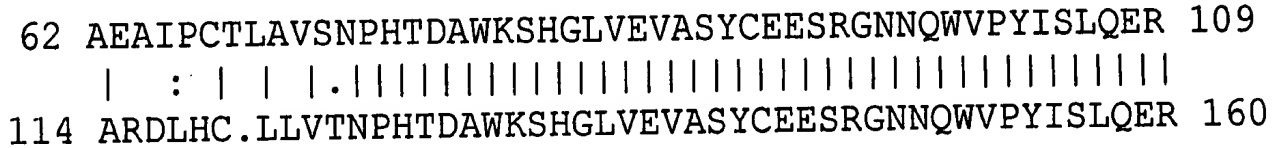
62 AEAIPCTLAVSNPHTDAWKSHGLVEVASYCEESRGNNQWVPYISLQER 109
114 ARDLHC.LLVTNPHTDAWKSHGLVEVASYCEESRGNNQWVPYISLQER 160

Fig. 6

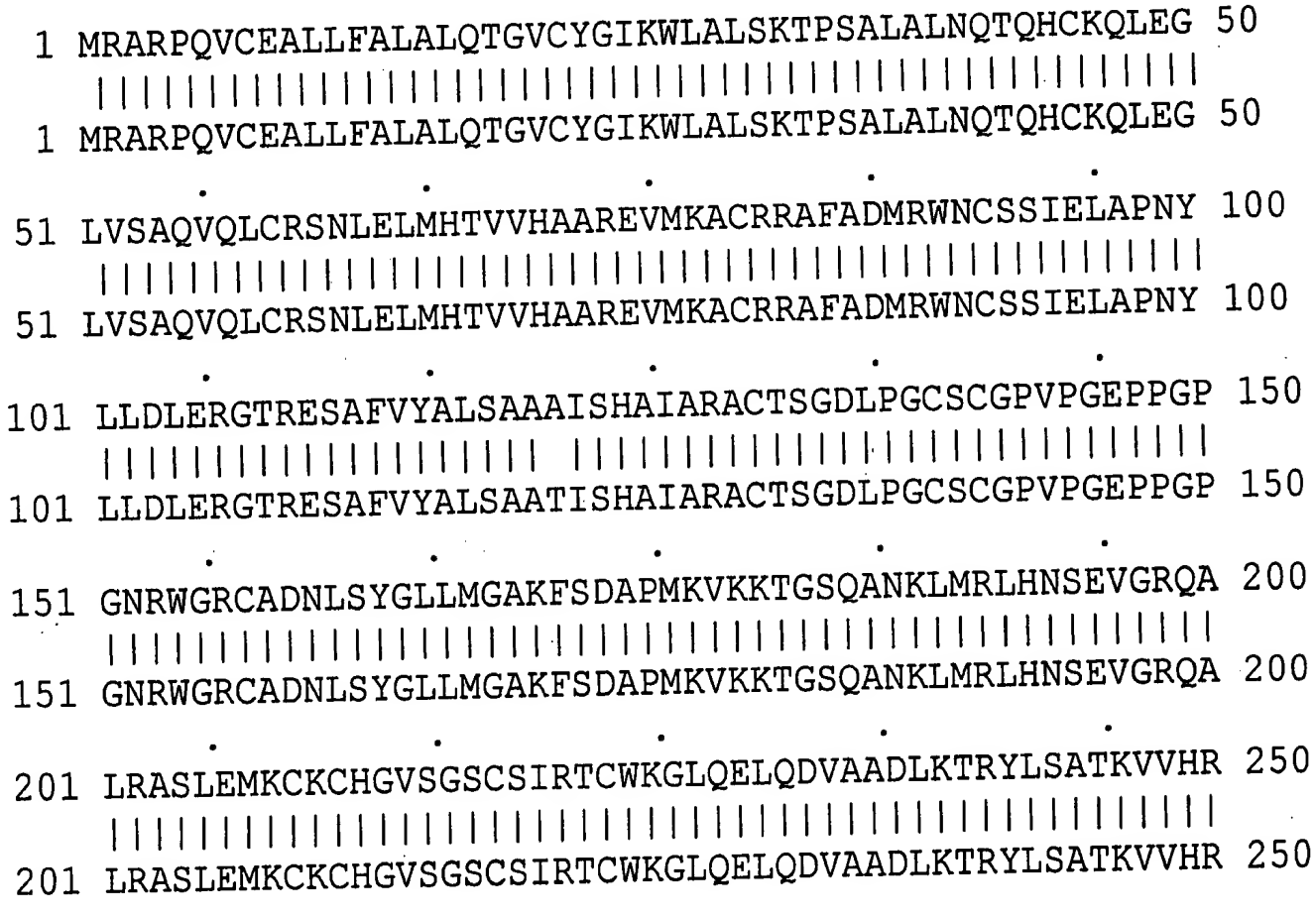
1 MRARPQVCEALLFALALQTGVCYGIKWLALSKTPSALALNQTQHCKQLEG 50
1 MRARPQVCEALLFALALQTGVCYGIKWLALSKTPSALALNQTQHCKQLEG 50
51 LVSAQVQLCRSNLELMHTVVHAAREVMKACRRAFADMRWNCSSIELAPNY 100
51 LVSAQVQLCRSNLELMHTVVHAAREVMKACRRAFADMRWNCSSIELAPNY 100
101 LLDLERGTRESAFVYALSAAAISHAIARACTSGDLPGCSCGPVPGEPPGP 150
101 LLDLERGTRESAFVYALSAATISHAIARACTSGDLPGCSCGPVPGEPPGP 150
151 GNRWGRCADNLSYGLLMGAKFSDAPMKVKKTGSQANKLMRLHNSEVGRQA 200
151 GNRWGRCADNLSYGLLMGAKFSDAPMKVKKTGSQANKLMRLHNSEVGRQA 200
201 LRASLEMKCKCHGVSGSCSIRTCWKGLQELQDVAADLKTRYLSATKVVHR 250
201 LRASLEMKCKCHGVSGSCSIRTCWKGLQELQDVAADLKTRYLSATKVVHR 250

Fig. 7

```
251 PMGTRKHLVPKDLDIRPVKDSELVYLQSSPDFCMKNEKVGSHGTQDRQCN 300
    |||||||||||||||||| ||||||||||||||||||||||||||||||
251 PMGTRKHLVPKDLDIRPVKDWELVYLQSSPDFCMKNEKVGSHGTQDRQCN 300
      .         .         .         .         .
301 KTSNGSDSCDLM.....................CCYVTCRRCERTVER 327
    ||||||||||||                     ||||||||||||||||
301 KTSNGSDSCDLMCCGRGYNPYTDRVVERCHCKYHWCCYVTCRRCERTVER 350

                328 YVCK 331
                    ||||
                351 YVCK 354
```

Fig. 7(Cont.)

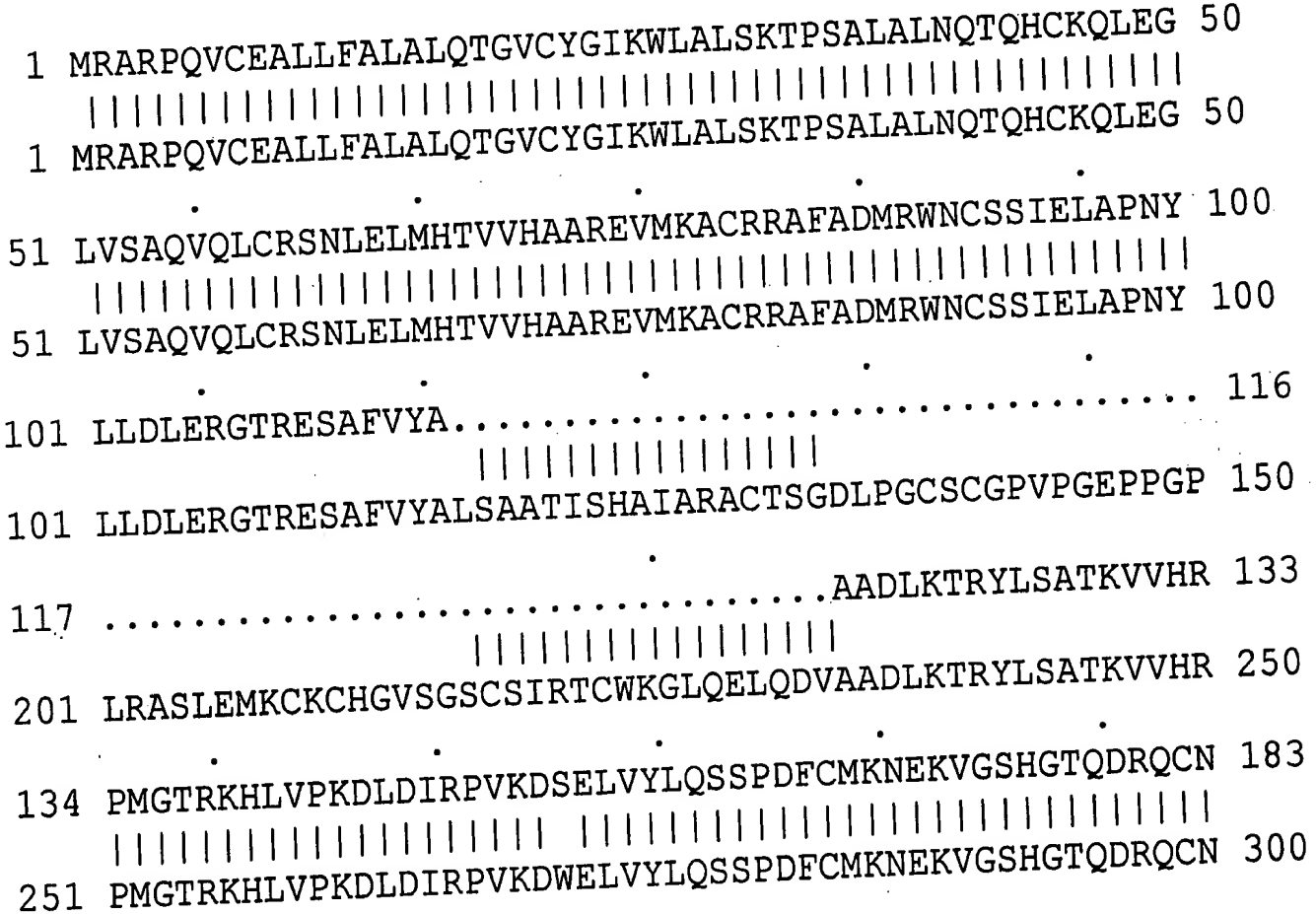

Fig. 8

```
184 KTSNGSDSCDLMCCGRGYNPYTDRVVERCHCKYHWCCYVTCRRCERTVER 233
    ||||||||||||||||||||||||||||||||||||||||||||||||||
301 KTSNGSDSCDLMCCGRGYNPYTDRVVERCHCKYHWCCYVTCRRCERTVER 350

234 YVCK 237
    ||||
351 YVCK 354
```

Fig. 8(Cont.)

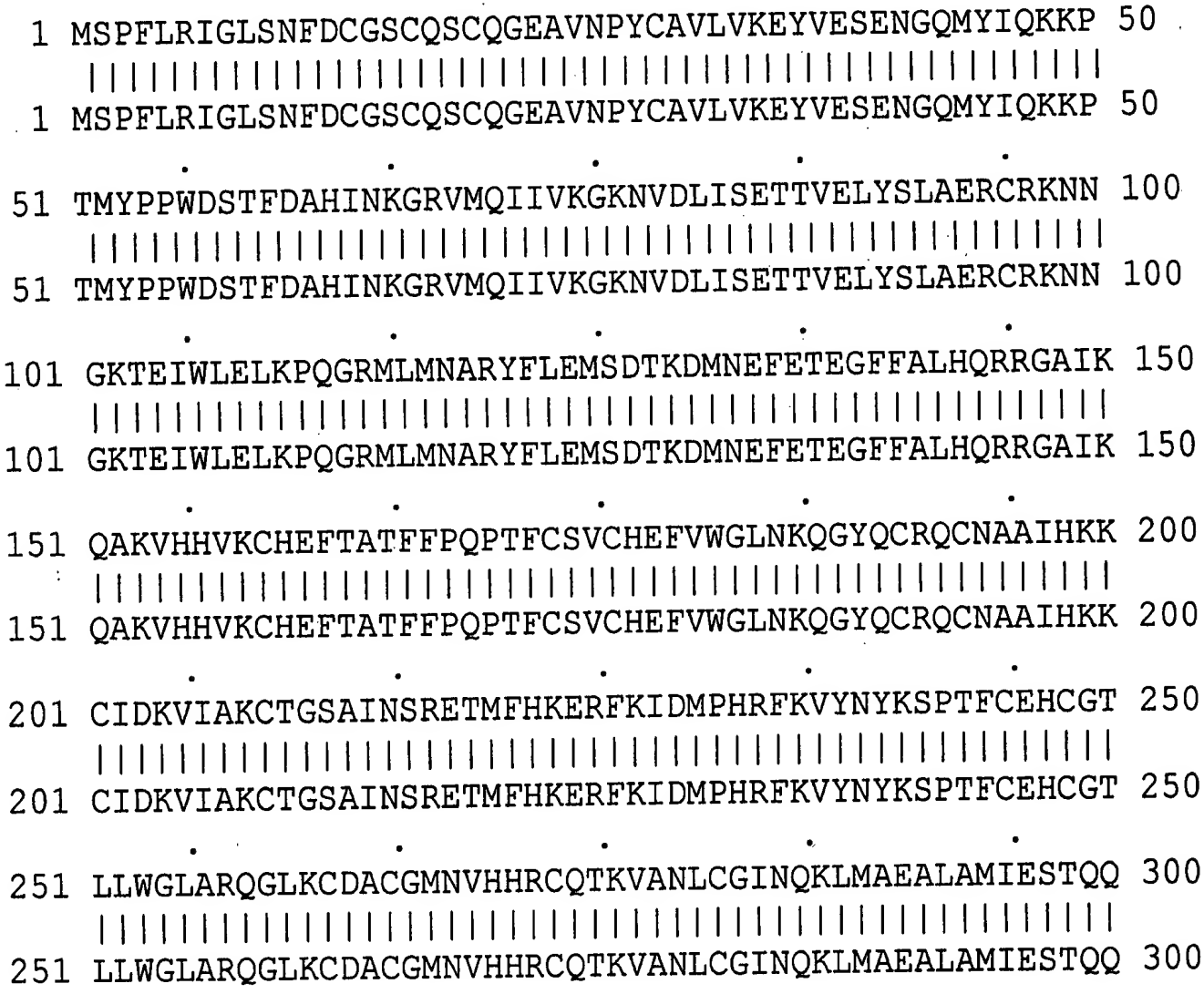

Fig. 9

```
301 ARCLRDTEQIFREGPVEIGLPCSIKNEARPPCLPTPGKREPQGISWESPL 350
    |||||||||||||||||||||||||||| ||||||||||||||||||||
301 ARCLRDTEQIFREGPVEIGLPCSIKNEARLPCLPTPGKREPQGISWESPL 350

351 DEVDKMCHLPEPELNKERPSLQIKLKIEDFILHKMLGKGSFGKVFLAEFK 400
    |||||||||||||||||||||||||||||||||||||||||||||||||
351 DEVDKMCHLPEPELNKERPSLQIKLKIEDFILHKMLGKGSFGKVFLAEFK 400

401 KTNQFFAIKALKKDVVLMDDDVECTMVEKRVLSLAWEHPFLTHMFCTFQT 450
    |||||||||||||||||||||||||||||||||||||||||||||||||
401 KTNQFFAIKALKKDVVLMDDDVECTMVEKRVLSLAWEHPFLTHMFCTFQT 450

451 KENLFFVMEYLNGGDLMYHIQSCHKFDLSRATFYAAEIILGLQFLHSKGI 500
    |||||||||||||||||||||||||||||||||||||||||||||||||
451 KENLFFVMEYLNGGDLMYHIQSCHKFDLSRATFYAAEIILGLQFLHSKGI 500

501 VYRDLKLDNILLDKDGHIKIADFGMCKENMLGDAKTNTFCGTPDYIAPEI 550
    |||||||||||||||||||||||||||||||||||||||||||||||||
501 VYRDLKLDNILLDKDGHIKIADFGMCKENMLGDAKTNTFCGTPDYIAPEI 550
```

Fig. 9(Cont.)

```
551 LLGQKYNHSVDWWSFGVLLYEMLIGQSPFHGQDEEELFHSIRMDNPFYPR 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||
551 LLGQKYNHSVDWWSFGVLLYEMLIGQSPFHGQDEEELFHSIRMDNPFYPR 600

601 WLEKEAKDLLVKV 613
    ||||||||||||.
601 WLEKEAKDLLVKL 613
```

Fig. 9(Cont.)

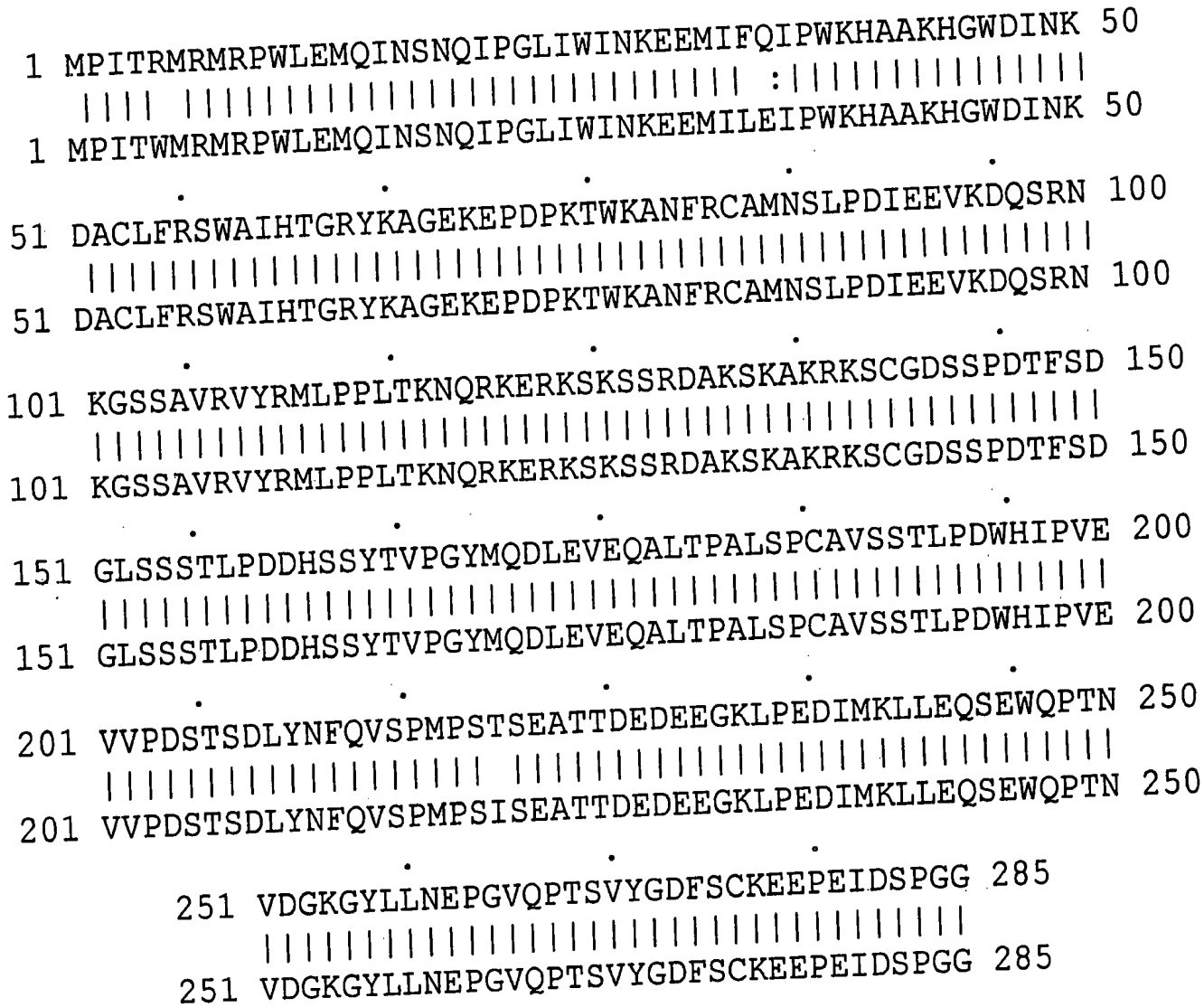
1 MPITRMRMRPWLEMQINSNQIPGLIWINKEEMIFQIPWKHAAKHGWDINK 50
1 MPITWMRMRPWLEMQINSNQIPGLIWINKEEMILEIPWKHAAKHGWDINK 50
51 DACLFRSWAIHTGRYKAGEKEPDPKTWKANFRCAMNSLPDIEEVKDQSRN 100
51 DACLFRSWAIHTGRYKAGEKEPDPKTWKANFRCAMNSLPDIEEVKDQSRN 100
101 KGSSAVRVYRMLPPLTKNQRKERKSKSSRDAKSKAKRKSCGDSSPDTFSD 150
101 KGSSAVRVYRMLPPLTKNQRKERKSKSSRDAKSKAKRKSCGDSSPDTFSD 150
151 GLSSSTLPDDHSSYTVPGYMQDLEVEQALTPALSPCAVSSTLPDWHIPVE 200
151 GLSSSTLPDDHSSYTVPGYMQDLEVEQALTPALSPCAVSSTLPDWHIPVE 200
201 VVPDSTSDLYNFQVSPMPSTSEATTDEDEEGKLPEDIMKLLEQSEWQPTN 250
201 VVPDSTSDLYNFQVSPMPSISEATTDEDEEGKLPEDIMKLLEQSEWQPTN 250
251 VDGKGYLLNEPGVQPTSVYGDFSCKEEPEIDSPGG 285
251 VDGKGYLLNEPGVQPTSVYGDFSCKEEPEIDSPGG 285

Fig. 10

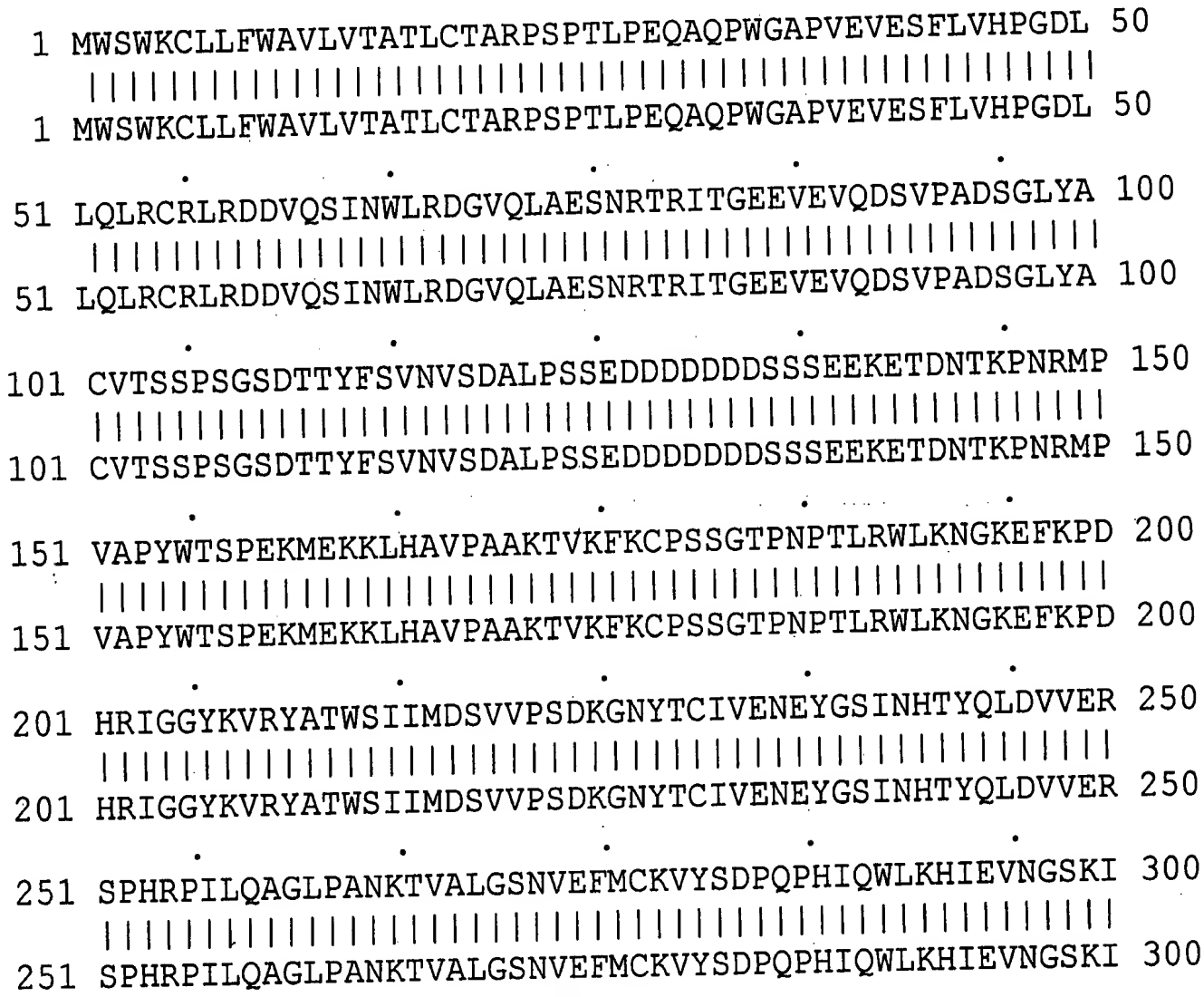

Fig. 11

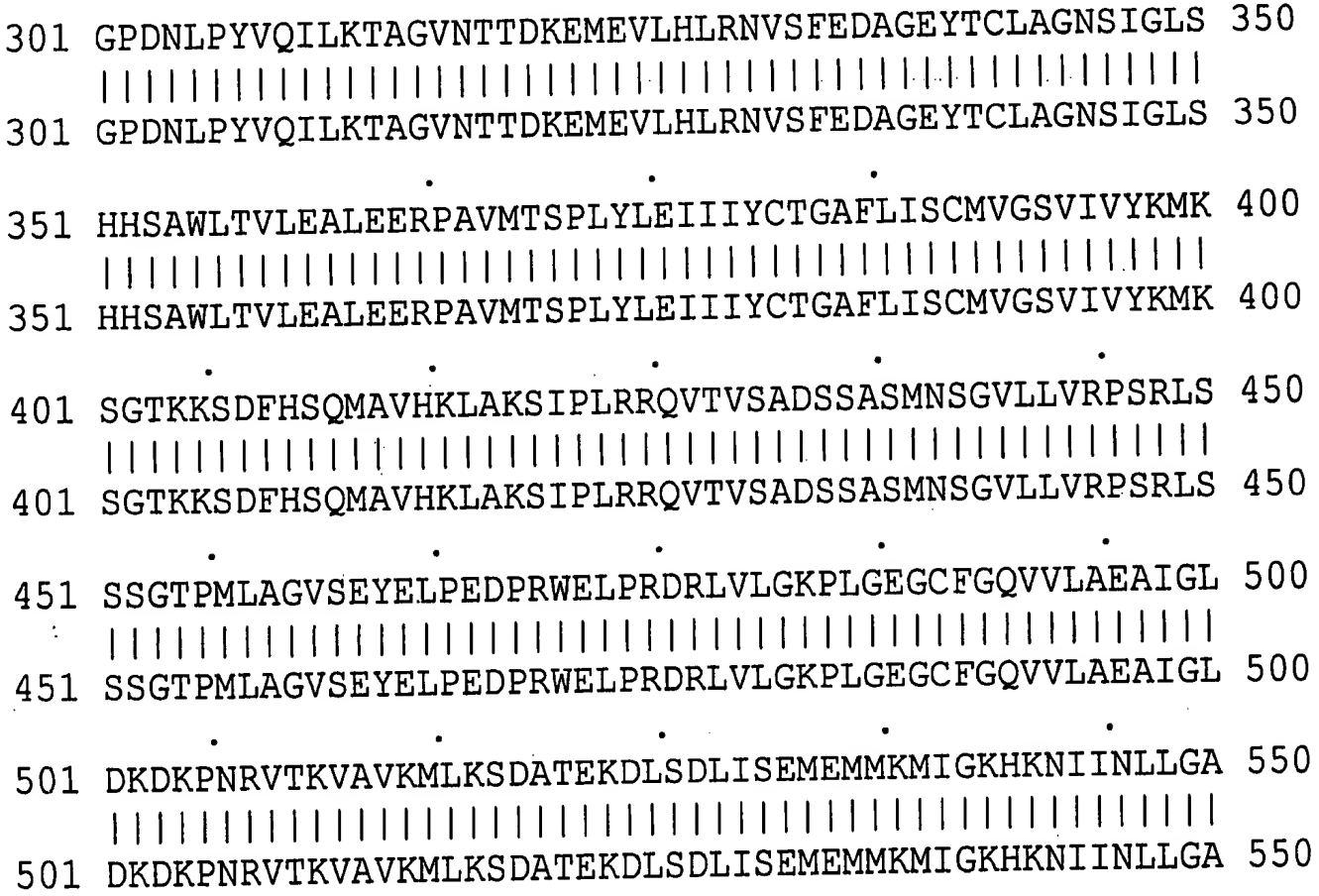

Fig. 11(Cont.)

```
551 CTQDGPLYVIVEYASKGNLREYLQARRPPGLEYCYNPSHNPEEQLSSKDL 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
551 CTQDGPLYVIVEYASKGNLREYLQARRPPGLEYCYNPSHNPEEQLSSKDL 600

601 VSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHH 650
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
601 VSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHH 650

      651 IDYYKKTTNGRLPVKWMAPEALFDRIYTHQSDVWSFGV 688
          |||||||||||||||||||||||||||||||||||||||
      651 IDYYKKTTNGRLPVKWMAPEALFDRIYTHQSDVWSFGV 688
```

Fig. 11(Cont.)

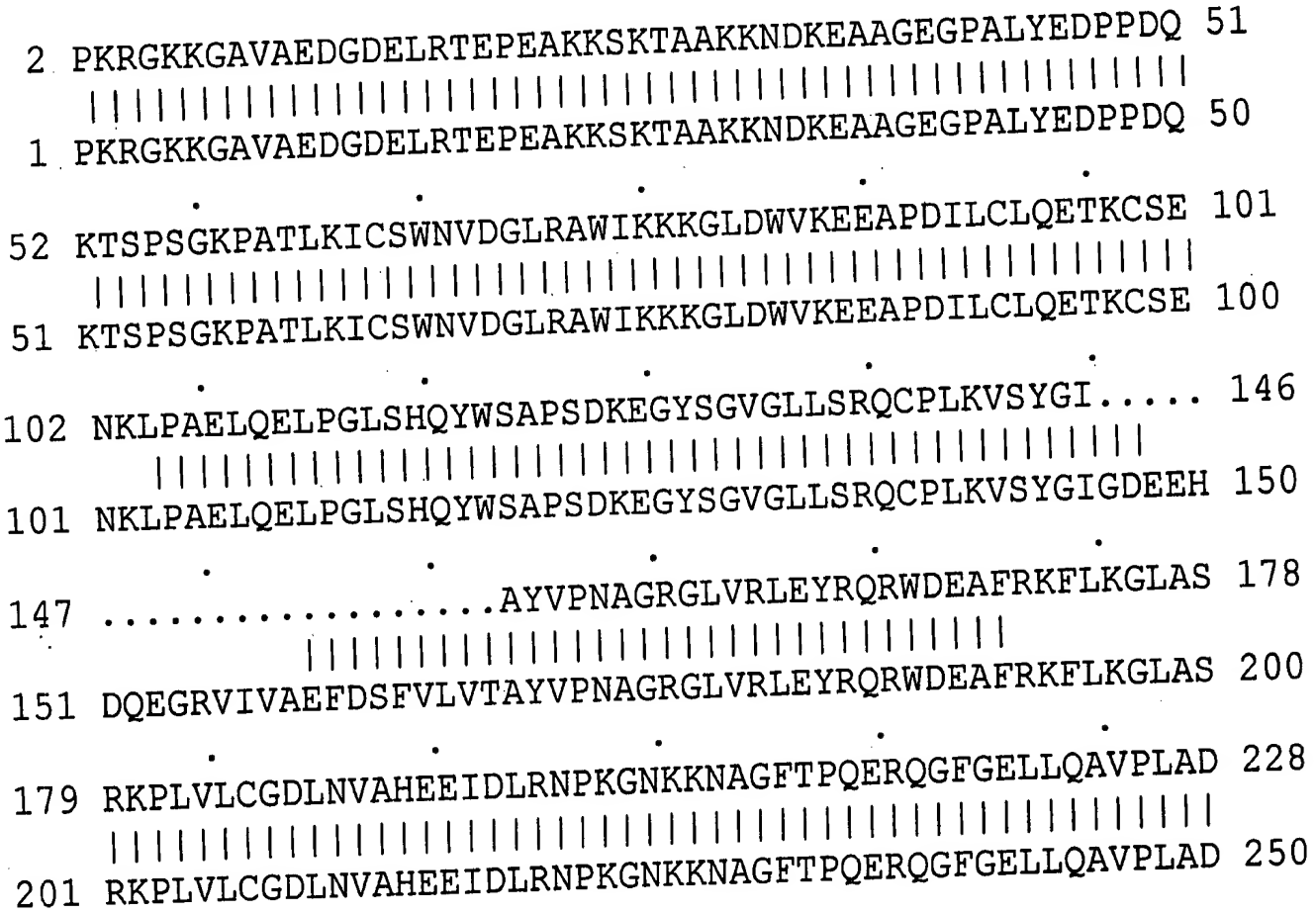

Fig. 12

```
229 SFRHLYPNTPYAYTFWTYMMNARSKNVGWRLDYFLLSHSLLPALCDSKIR 278
    |||||||||||||||||||||||||||||||||||||||||||||||||||
251 SFRHLYPNTPYAYTFWTYMMNARSKNVGWRLDYFLLSHSLLPALCDSKIR 300
```

```
279 SKALGSDHCPITLYLAL 295
    |||||||||||||||||
301 SKALGSDHCPITLYLAL 317
```

Fig. 12(Cont.)

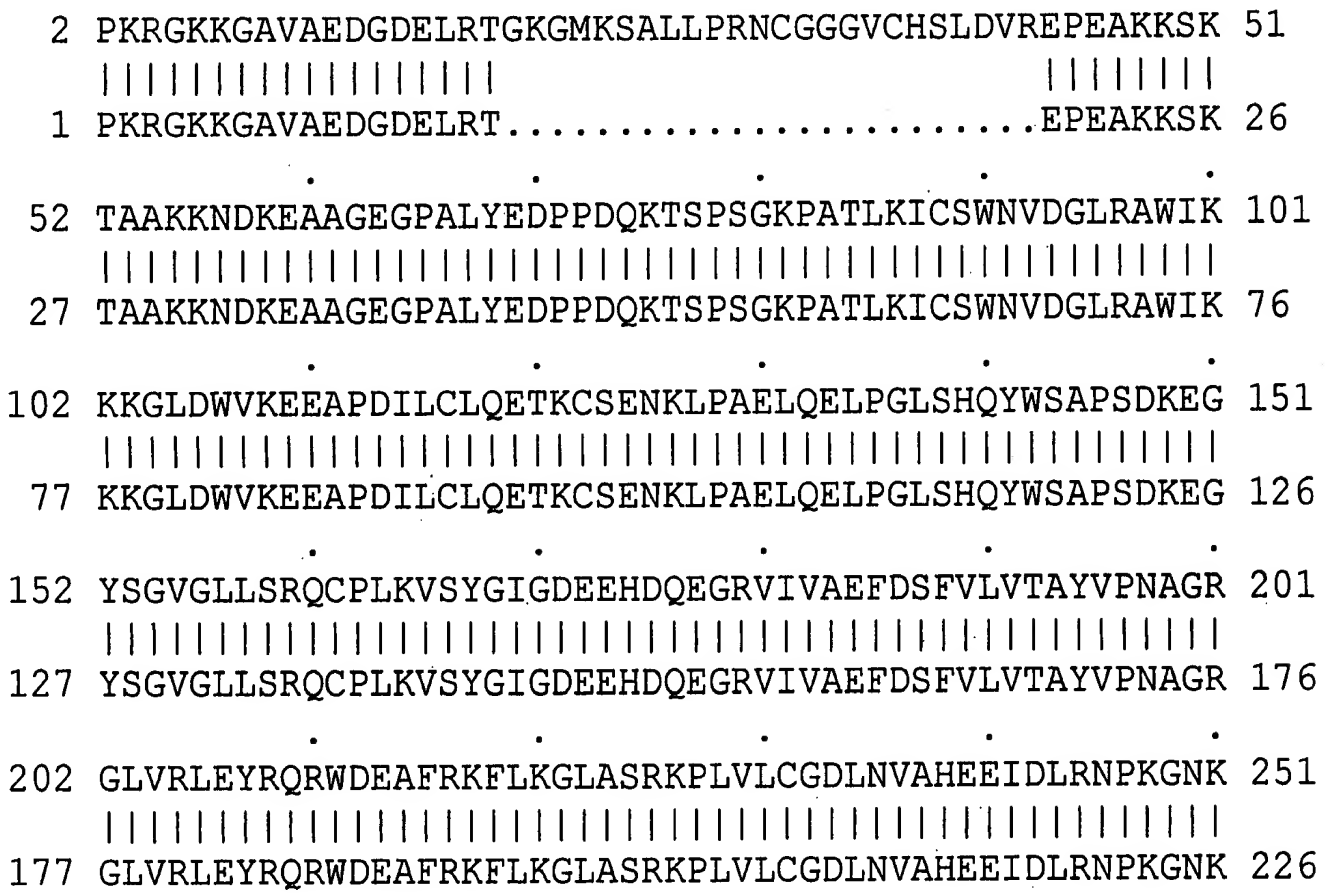

Fig. 13

```
252 KNAGFTPQERQGFGELLQAVPLADSFRHLYPNTPYAYTFWTYMMNARSKN 301
    ||||||||||||||||||||||||||||||||||||||||||||||||||
227 KNAGFTPQERQGFGELLQAVPLADSFRHLYPNTPYAYTFWTYMMNARSKN 276

302 VGWRLDYFLLSHSLLPALCDSKIRSKALGSDHCPITLYLAL 342
    |||||||||||||||||||||||||||||||||||||||||
277 VGWRLDYFLLSHSLLPALCDSKIRSKALGSDHCPITLYLAL 317
```

Fig. 13(Cont.)

```
1 MFQAAERPQEWAMEGPRDGLKKERLLDDRHDSGLDSMKDEEYEQMVKELQ 50
  ||||||||||||||||||||||||||||||||||||||||||||||||||
1 MFQAAERPQEWAMEGPRDGLKKERLLDDRHDSGLDSMKDEEYEQMVKELQ 50

51 EIRLEPQEVPRGSEPWKQQLTEDGDSFLHLAIIHEEKALTMEVIRQVKGD 100
   ||||||||||||||||||||||||||||||||||||||||||||||||||
51 EIRLEPQEVPRGSEPWKQQLTEDGDSFLHLAIIHEEKALTMEVIRQVKGD 100

101 LAFLNFQNNLQQTPLHLAVITNQPEIAEALLGAGCDPELRDFRGNTPLHL 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 LAFLNFQNNLQQTPLHLAVITNQPEIAEALLGAGCDPELRDFRGNTPLHL 150

151 ACEQGCLASVGVLTQSCTTPHLHSILKATNYNGHTCLHLASIHGYLGIVE 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 ACEQGCLASVGVLTQSCTTPHLHSILKATNYNGHTCLHLASIHGYLGIVE 200

201 LLVSLGADVNAQEPCNGRTALHLAVDLQNPDLVSLLLKCGADVNRVTYQG 250
    ||||||||||||||||||||||||||||||||||||||||||||||||||
201 LLVSLGADVNAQEPCNGRTALHLAVDLQNPDLVSLLLKCGADVNRVTYQG 250
```

Fig. 14

```
251 YSPYQLTWGRPSTRIQQQLGQLTLENLQMLPESEDEESYDTESEFTEFTE 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
251 YSPYQLTWGRPSTRIQQQLGQLTLENLQMLPESEDEESYDTESEFTEFTE 300

                    301 DEV 303
                        ||.
                    301 DEL 303
```

Fig. 14 (Cont.)

```
1 MFQAAERPQEWAMEGPRDGLKKERLLDDRHDSGLDSMKDEEYEQMVKELQ 50
  |||||||||||||||||||||||||||||||||||||||||||||||||||
1 MFQAAERPQEWAMEGPRDGLKKERLLDDRHDSGLDSMKDEEYEQMVKELQ 50

51 EIRLEPQEVPRGSEPWKQQLTEDGDSFLHLAIIHEEKALTMEVIRQVKGD 100
   |||||||||||||||||||||||||||||||||||||||||||||||||||
51 EIRLEPQEVPRGSEPWKQQLTEDGDSFLHLAIIHEEKALTMEVIRQVKGD 100

101 LAFLNFQNNLQQTPLHLAVITNQPEIAEALLGAGCDPELRDFRGNTPLHL 150
    |||||||||||||||||||||||||||||||||||||||||||||||||||
101 LAFLNFQNNLQQTPLHLAVITNQPEIAEALLGAGCDPELRDFRGNTPLHL 150

151 ACEQGCLASVGVLTQSCTTPHLHSILKATNYNG..................  183
    ||||||||||||||||||||||||||||||||
151 ACEQGCLASVGVLTQSCTTPHLHSILKATNYNGHTCLHLASIHGYLGIVE 200

151 ACEQGCLASVGVLTQSCTTPHLHSILKATNYNGHTCLHLASIHGYLGIVE 222

184 .....QEPCNGRTALHLAVDLQNPDLVSLLLKCGADVNRVTYQG 250
          ||||||||||||||||||||||||||||||||||||||||
201 LLVSLGADVNAQEPCNGRTALHLAVDLQNPDLVSLLLKCGADVNRVTYQG 250
```

Fig. 15

```
223 YSPYQLTWGRPSTRIQQQLGQLTLENLQMLPESEDEESYDTESEFTEFTE 272
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
251 YSPYQLTWGRPSTRIQQQLGQLTLENLQMLPESEDEESYDTESEFTEFTE 300

273 DELPYDDCVFGGQRLTL 289
    |||||||||||||||||
301 DELPYDDCVFGGQRLTL 317
```

Fig. 15(Cont.)

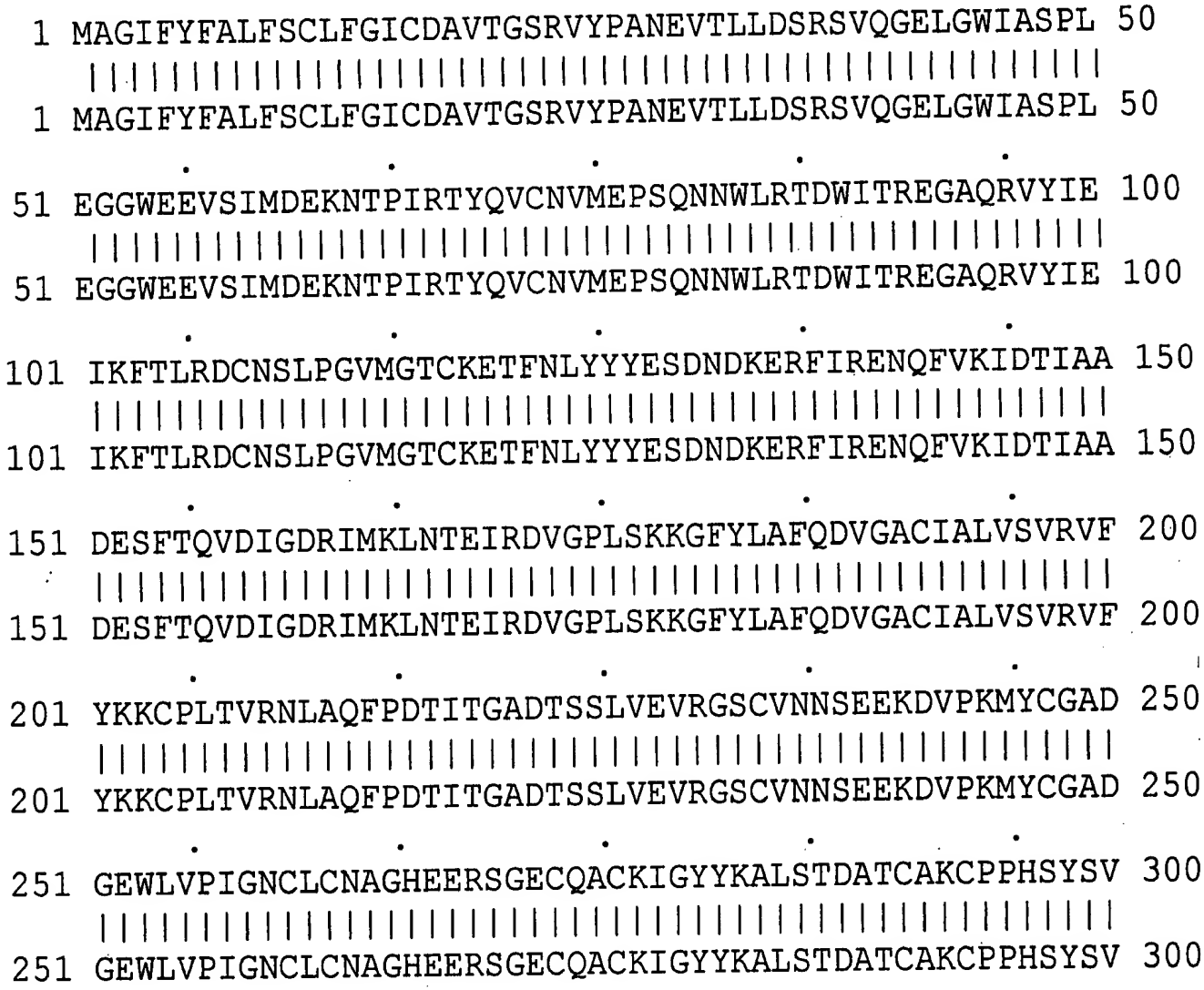
1 MAGIFYFALFSCLFGICDAVTGSRVYPANEVTLLDSRSVQGELGWIASPL 50
1 MAGIFYFALFSCLFGICDAVTGSRVYPANEVTLLDSRSVQGELGWIASPL 50
51 EGGWEEVSIMDEKNTPIRTYQVCNVMEPSQNNWLRTDWITREGAQRVYIE 100
51 EGGWEEVSIMDEKNTPIRTYQVCNVMEPSQNNWLRTDWITREGAQRVYIE 100
101 IKFTLRDCNSLPGVMGTCKETFNLYYYESDNDKERFIRENQFVKIDTIAA 150
101 IKFTLRDCNSLPGVMGTCKETFNLYYYESDNDKERFIRENQFVKIDTIAA 150
151 DESFTQVDIGDRIMKLNTEIRDVGPLSKKGFYLAFQDVGACIALVSVRVF 200
151 DESFTQVDIGDRIMKLNTEIRDVGPLSKKGFYLAFQDVGACIALVSVRVF 200
201 YKKCPLTVRNLAQFPDTITGADTSSLVEVRGSCVNNSEEKDVPKMYCGAD 250
201 YKKCPLTVRNLAQFPDTITGADTSSLVEVRGSCVNNSEEKDVPKMYCGAD 250
251 GEWLVPIGNCLCNAGHEERSGECQACKIGYYKALSTDATCAKCPPHSYSV 300
251 GEWLVPIGNCLCNAGHEERSGECQACKIGYYKALSTDATCAKCPPHSYSV 300

Fig. 16

```
301 WEGATSCTCDRGFFRADNDAASMPCTRPPSAPLNLISNVNETSVNLEWSS 350
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
301 WEGATSCTCDRGFFRADNDAASMPCTRPPSAPLNLISNVNETSVNLEWSS 350

351 PQNTGGRQDISYNVVCKKCGAGDPSKCRPCGSGVHYTPQQNGLKTTKVSI 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
351 PQNTGGRQDISYNVVCKKCGAGDPSKCRPCGSGVHYTPQQNGLKTTKVSI 400

401 TDLLAHTNYTFEIWAVNGVSKYNPNPDQSVSVTVTTNQAAPSSIALVQAK 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
401 TDLLAHTNYTFEIWAVNGVSKYNPNPDQSVSVTVTTNQAAPSSIALVQAK 450

451 EVTRYSVALAWLEPDRPNGVILEYEVKYYEKDQNERSYRIVRTAARNTDI 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
451 EVTRYSVALAWLEPDRPNGVILEYEVKYYEKDQNERSYRIVRTAARNTDI 500

501 KGLNPLTSYVFHVRARTAAGYGDFSEPLEVTTNTVPSRIIGDGANSTVLL 550
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
501 KGLNPLTSYVFHVRARTAAGYGDFSEPLEVTTNTVPSRIIGDGANSTVLL 550

551 VSVSGSVVLVVILIAAFVISRRRSKYSKAKQEADEEKHLNQGVRTYVDPF 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
551 VSVSGSVVLVVILIAAFVISRRRSKYSKAKQEADEEKHLNQGVRTYVDPF 600
```

Fig. 16(Cont.)

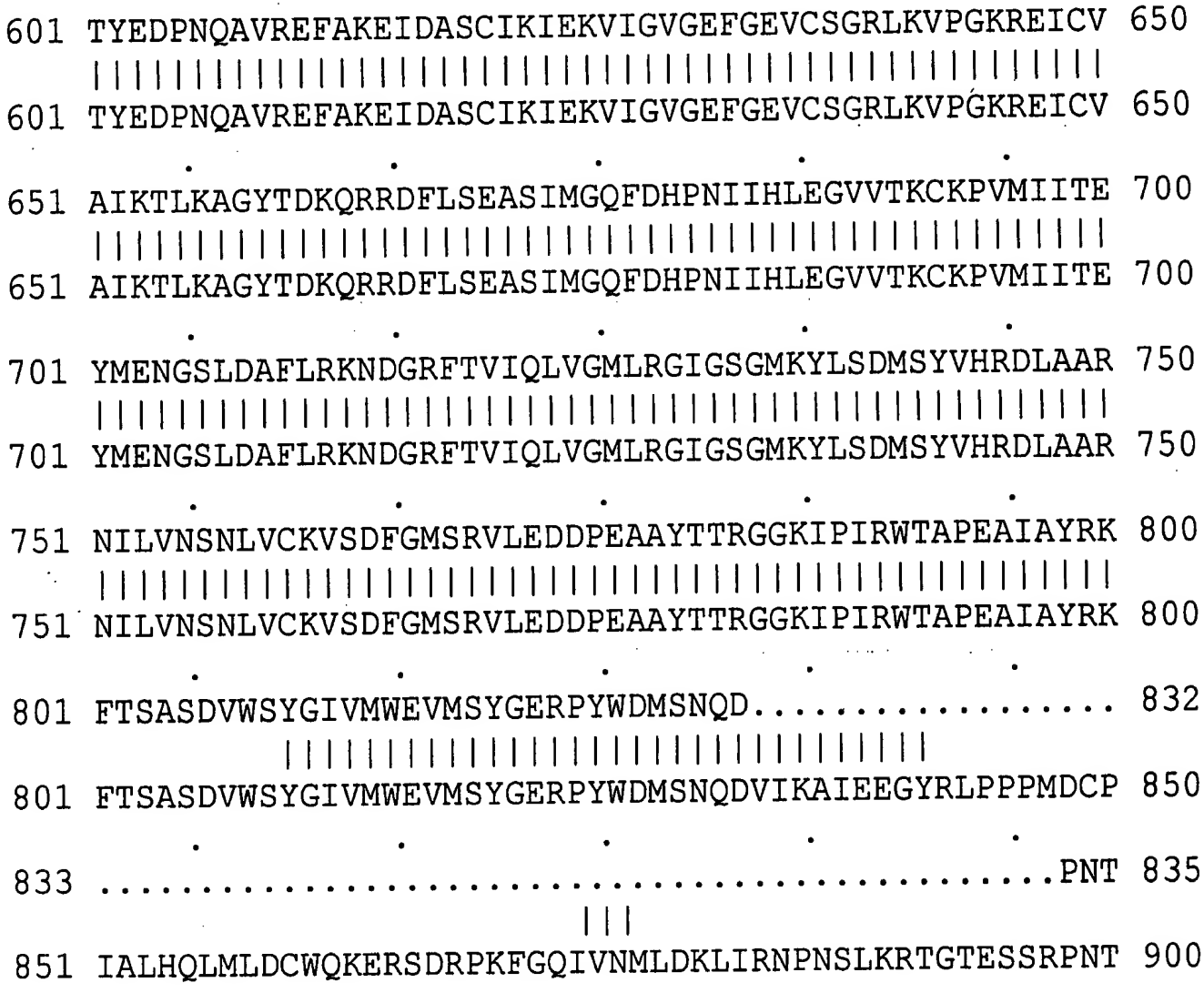

Fig. 16(Cont.)

```
836 ALLDPSSPEFSAVVSVGDWLQAIKMDRYKDNFTAAGYTTLEAVVHVNQED 885
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
901 ALLDPSSPEFSAVVSVGDWLQAIKMDRYKDNFTAAGYTTLEAVVHVNQED 950

886 LARIGITAITHQNKILSSVQAMRTQMQQMHGRMVPV 921
    |||||||||||||||||||||||||||||||||||||
951 LARIGITAITHQNKILSSVQAMRTQMQQMHGRMVPV 986
```

Fig. 16(Cont.)

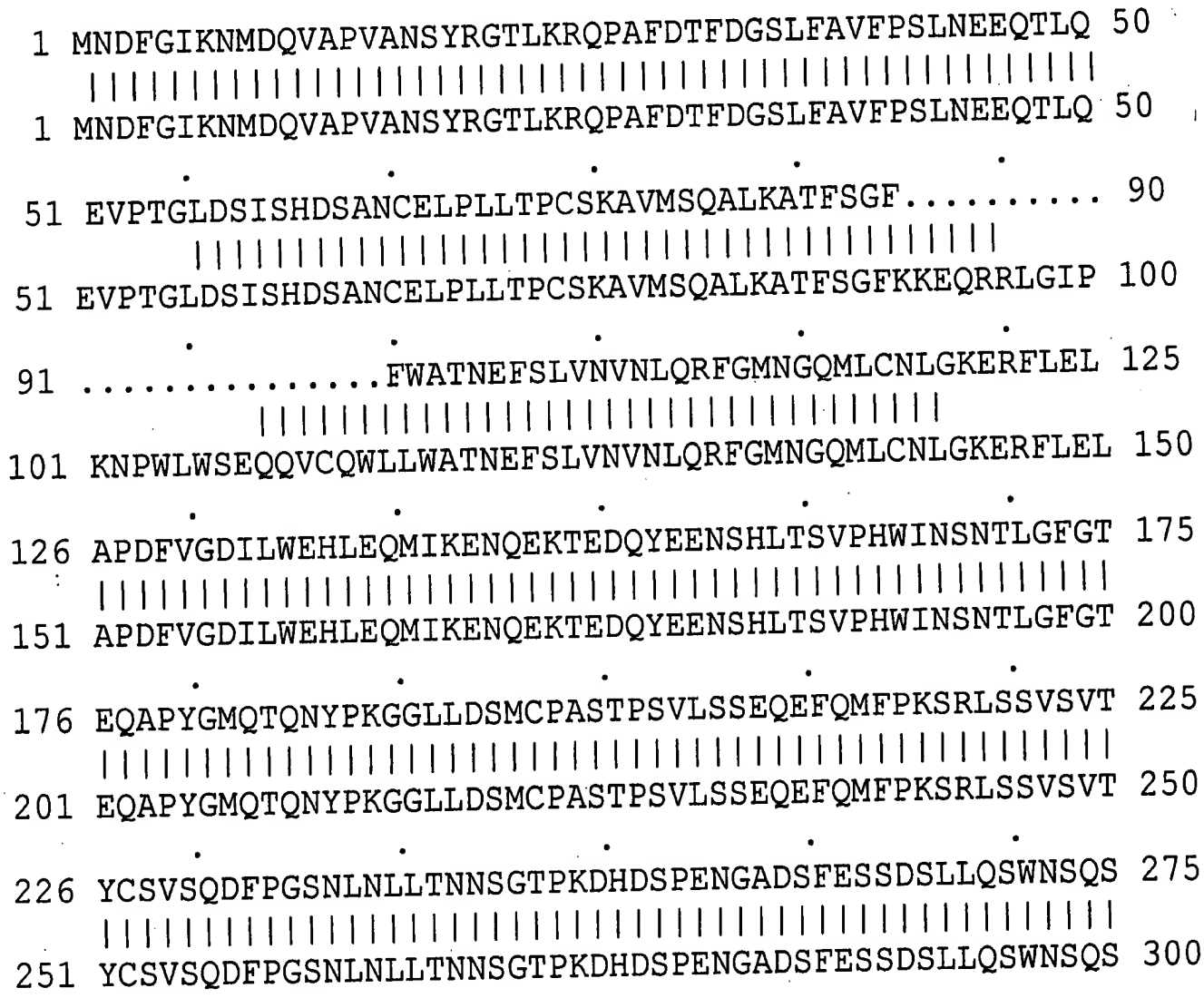
1 MNDFGIKNMDQVAPVANSYRGTLKRQPAFDTFDGSLFAVFPSLNEEQTLQ 50
1 MNDFGIKNMDQVAPVANSYRGTLKRQPAFDTFDGSLFAVFPSLNEEQTLQ 50
51 EVPTGLDSISHDSANCELPLLTPCSKAVMSQALKATFSGF..... 90
51 EVPTGLDSISHDSANCELPLLTPCSKAVMSQALKATFSGFKKEQRRLGIP 100
91 .....FWATNEFSLVNVNLQRFGMNGQMLCNLGKERFLEL 125
101 KNPWLWSEQQVCQWLLWATNEFSLVNVNLQRFGMNGQMLCNLGKERFLEL 150
126 APDFVGDILWEHLEQMIKENQEKTEDQYEENSHLTSVPHWINSNTLGFGT 175
151 APDFVGDILWEHLEQMIKENQEKTEDQYEENSHLTSVPHWINSNTLGFGT 200
176 EQAPYGMQTQNYPKGGLLDSMCPASTPSVLSSEQEFQMFPKSRLSSVSVT 225
201 EQAPYGMQTQNYPKGGLLDSMCPASTPSVLSSEQEFQMFPKSRLSSVSVT 250
226 YCSVSQDFPGSNLNLLTNNSGTPKDHDSPENGADSFESSDSLLQSWNSQS 275
251 YCSVSQDFPGSNLNLLTNNSGTPKDHDSPENGADSFESSDSLLQSWNSQS 300

Fig. 17

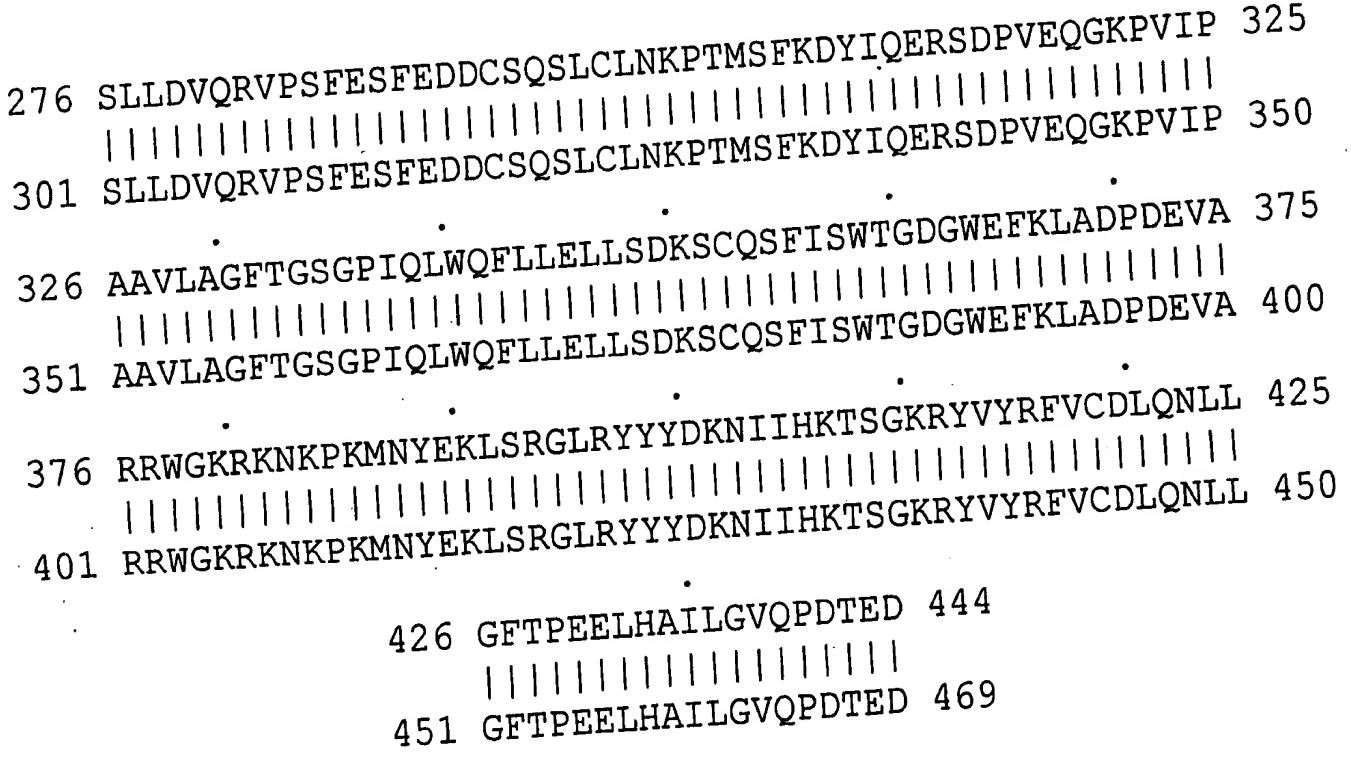
276 SLLDVQRVPSFESFEDDCSQSLCLNKPTMSFKDYIQERSDPVEQGKPVIP 325
301 SLLDVQRVPSFESFEDDCSQSLCLNKPTMSFKDYIQERSDPVEQGKPVIP 350
326 AAVLAGFTGSGPIQLWQFLLELLSDKSCQSFISWTGDGWEFKLADPDEVA 375
351 AAVLAGFTGSGPIQLWQFLLELLSDKSCQSFISWTGDGWEFKLADPDEVA 400
376 RRWGKRKNKPKMNYEKLSRGLRYYYDKNIIHKTSGKRYVYRFVCDLQNLL 425
401 RRWGKRKNKPKMNYEKLSRGLRYYYDKNIIHKTSGKRYVYRFVCDLQNLL 450
426 GFTPEELHAILGVQPDTED 444
451 GFTPEELHAILGVQPDTED 469

Fig. 17(Cont.)

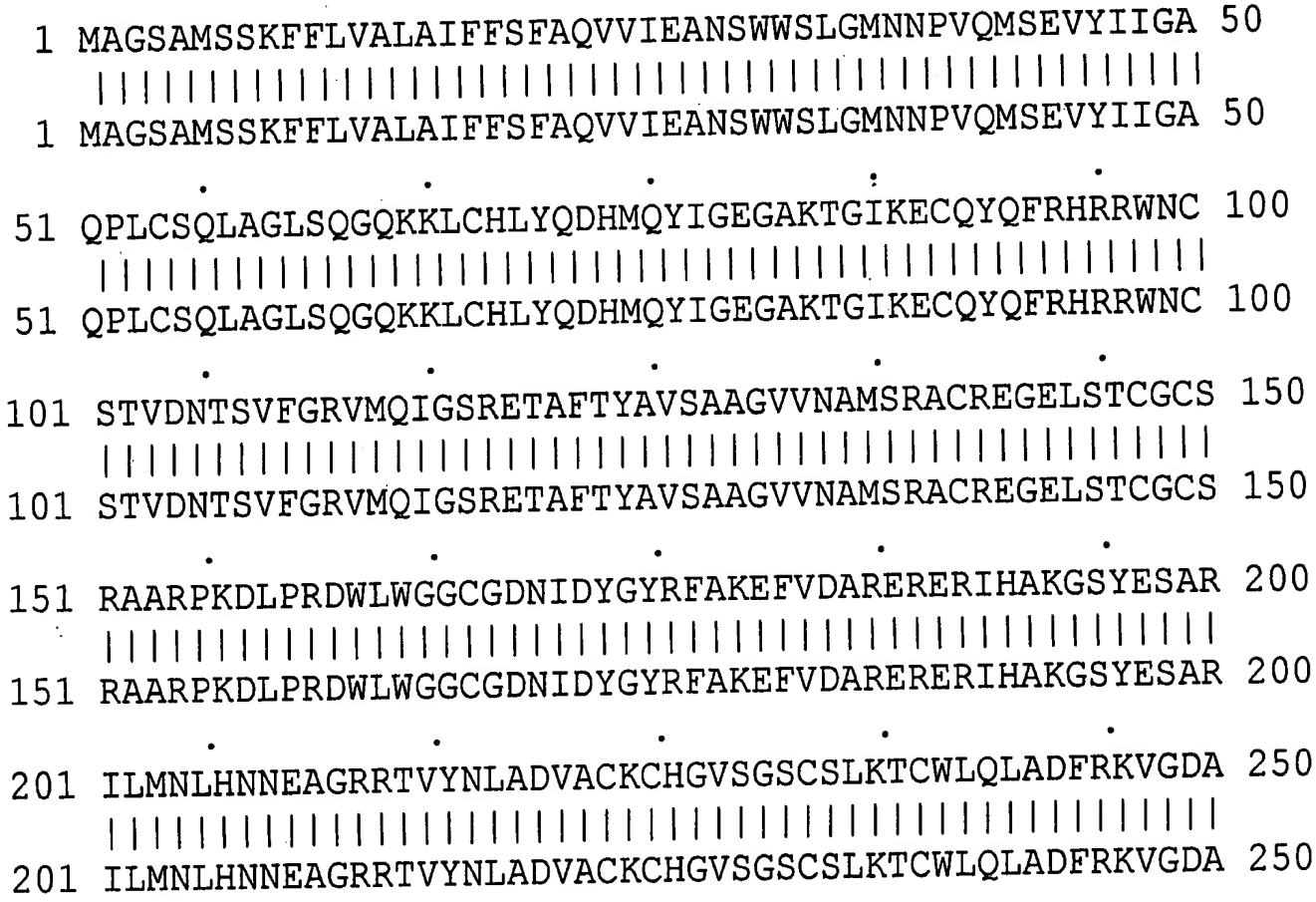
1 MAGSAMSSKFFLVALAIFFSFAQVVIEANSWWSLGMNNPVQMSEVYIIGA 50
1 MAGSAMSSKFFLVALAIFFSFAQVVIEANSWWSLGMNNPVQMSEVYIIGA 50
51 QPLCSQLAGLSQGQKKLCHLYQDHMQYIGEGAKTGIKECQYQFRHRRWNC 100
51 QPLCSQLAGLSQGQKKLCHLYQDHMQYIGEGAKTGIKECQYQFRHRRWNC 100
101 STVDNTSVFGRVMQIGSRETAFTYAVSAAGVVNAMSRACREGELSTCGCS 150
101 STVDNTSVFGRVMQIGSRETAFTYAVSAAGVVNAMSRACREGELSTCGCS 150
151 RAARPKDLPRDWLWGGCGDNIDYGYRFAKEFVDARERERIHAKGSYESAR 200
151 RAARPKDLPRDWLWGGCGDNIDYGYRFAKEFVDARERERIHAKGSYESAR 200
201 ILMNLHNNEAGRRTVYNLADVACKCHGVSGSCSLKTCWLQLADFRKVGDA 250
201 ILMNLHNNEAGRRTVYNLADVACKCHGVSGSCSLKTCWLQLADFRKVGDA 250
251 LKEKYDT 257
251 LKEKYDS 257

Fig. 18

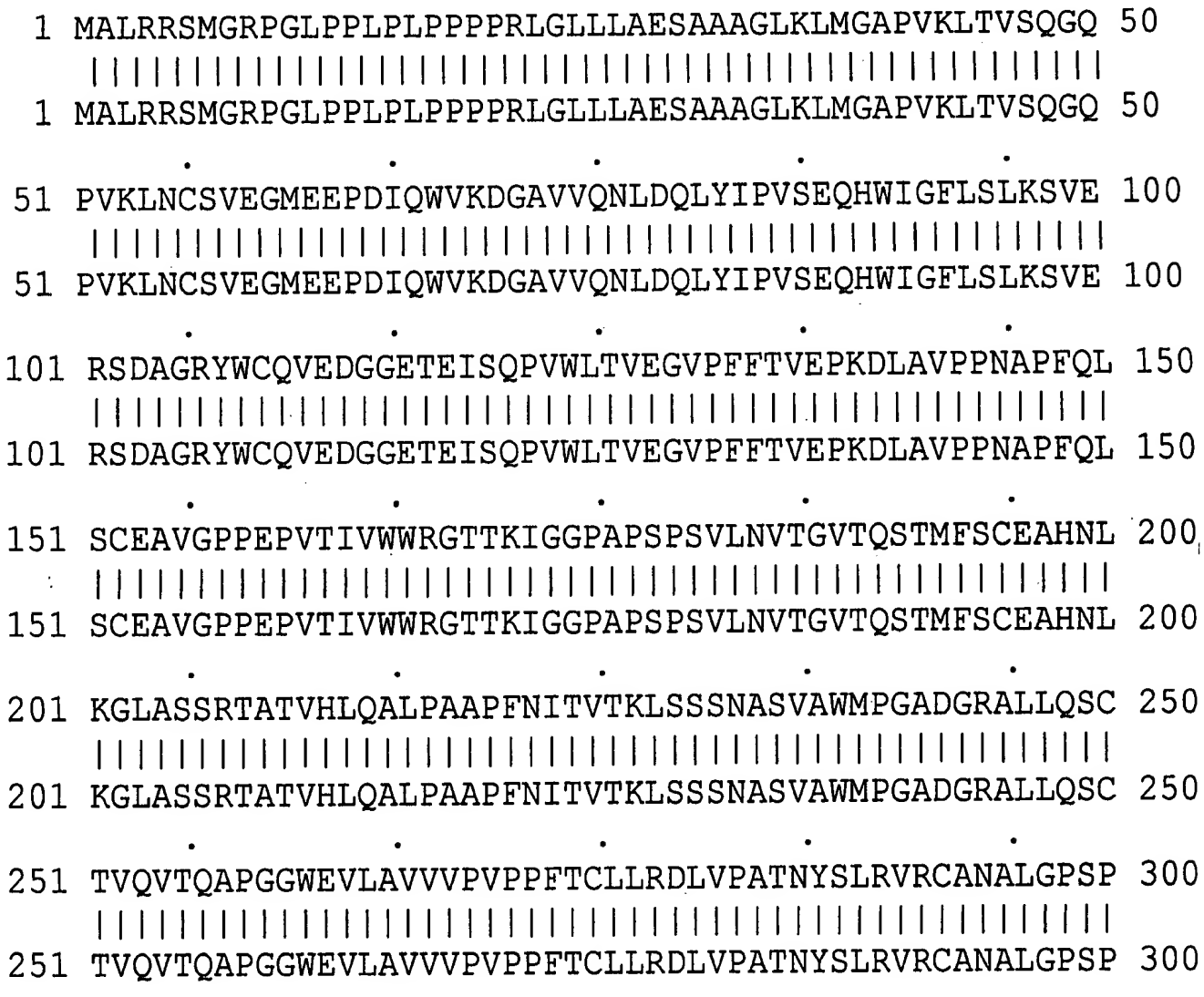

Fig. 19

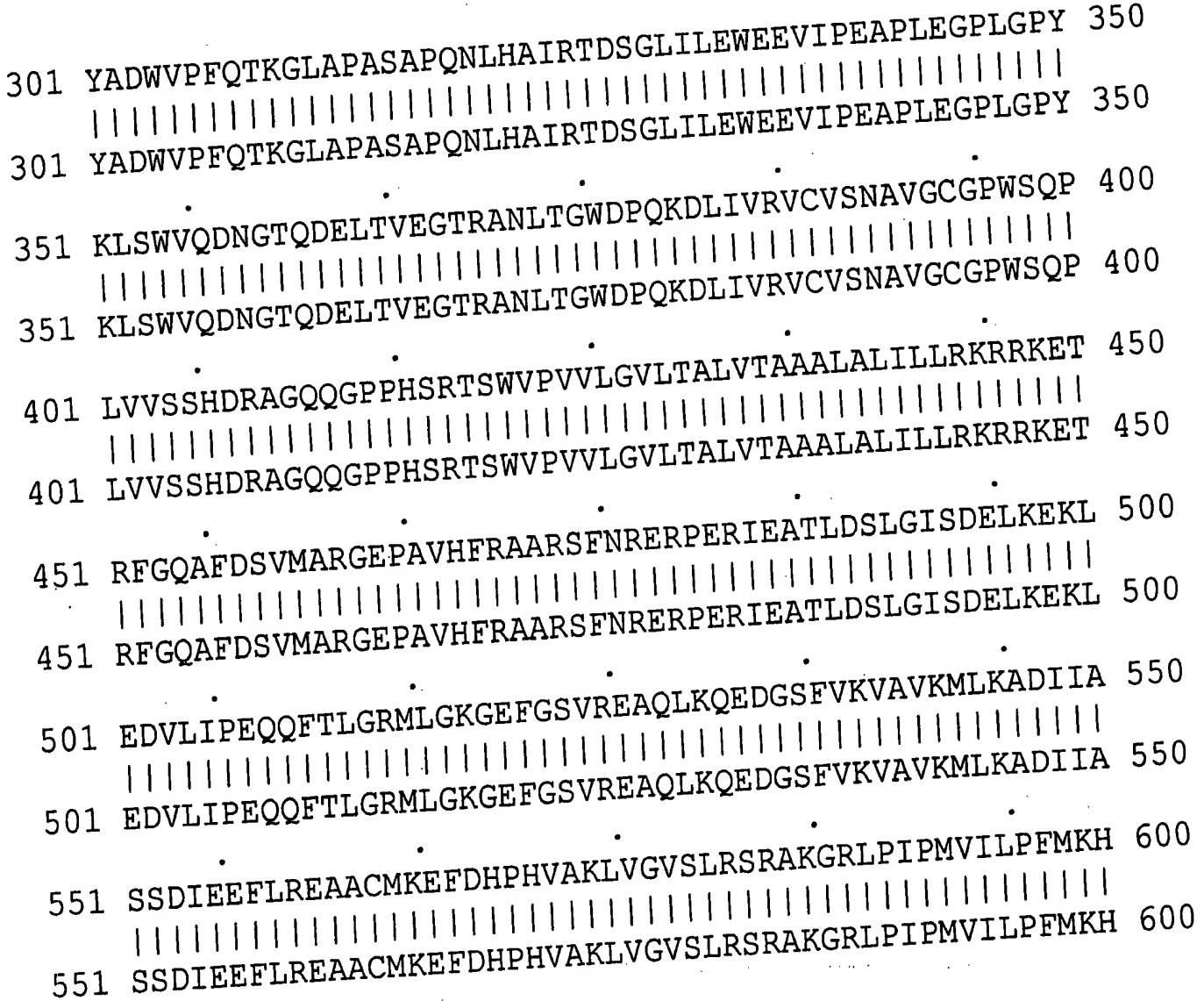
301 YADWVPFQTKGLAPASAPQNLHAIRTDSGLILEWEEVIPEAPLEGPLGPY 350
301 YADWVPFQTKGLAPASAPQNLHAIRTDSGLILEWEEVIPEAPLEGPLGPY 350
351 KLSWVQDNGTQDELTVEGTRANLTGWDPQKDLIVRVCVSNAVGCGPWSQP 400
351 KLSWVQDNGTQDELTVEGTRANLTGWDPQKDLIVRVCVSNAVGCGPWSQP 400
401 LVVSSHDRAGQQGPPHSRTSWVPVVLGVLTALVTAAALALILLRKRRKET 450
401 LVVSSHDRAGQQGPPHSRTSWVPVVLGVLTALVTAAALALILLRKRRKET 450
451 RFGQAFDSVMARGEPAVHFRAARSFNRERPERIEATLDSLGISDELKEKL 500
451 RFGQAFDSVMARGEPAVHFRAARSFNRERPERIEATLDSLGISDELKEKL 500
501 EDVLIPEQQFTLGRMLGKGEFGSVREAQLKQEDGSFVKVAVKMLKADIIA 550
501 EDVLIPEQQFTLGRMLGKGEFGSVREAQLKQEDGSFVKVAVKMLKADIIA 550
551 SSDIEEFLREAACMKEFDHPHVAKLVGVSLRSRAKGRLPIPMVILPFMKH 600
551 SSDIEEFLREAACMKEFDHPHVAKLVGVSLRSRAKGRLPIPMVILPFMKH 600

Fig. 19(Cont.)

```
601 GDLHAFLLASRIGENPFNLPLQTLIRFMVDIACGMEYLSSRNFIHRDLAA 650
    ||||||||||||||||||||||||||||||||||||||||||||||||||
601 GDLHAFLLASRIGENPFNLPLQTLIRFMVDIACGMEYLSSRNFIHRDLAA 650

651 RNCMLAEDMTVCVADFGLSRKIYSDCRY 678
    |||||||||||||||||||||||    |
651 RNCMLAEDMTVCVADFGLSRKIYSGDYY 678
```

Fig. 19(Cont.)

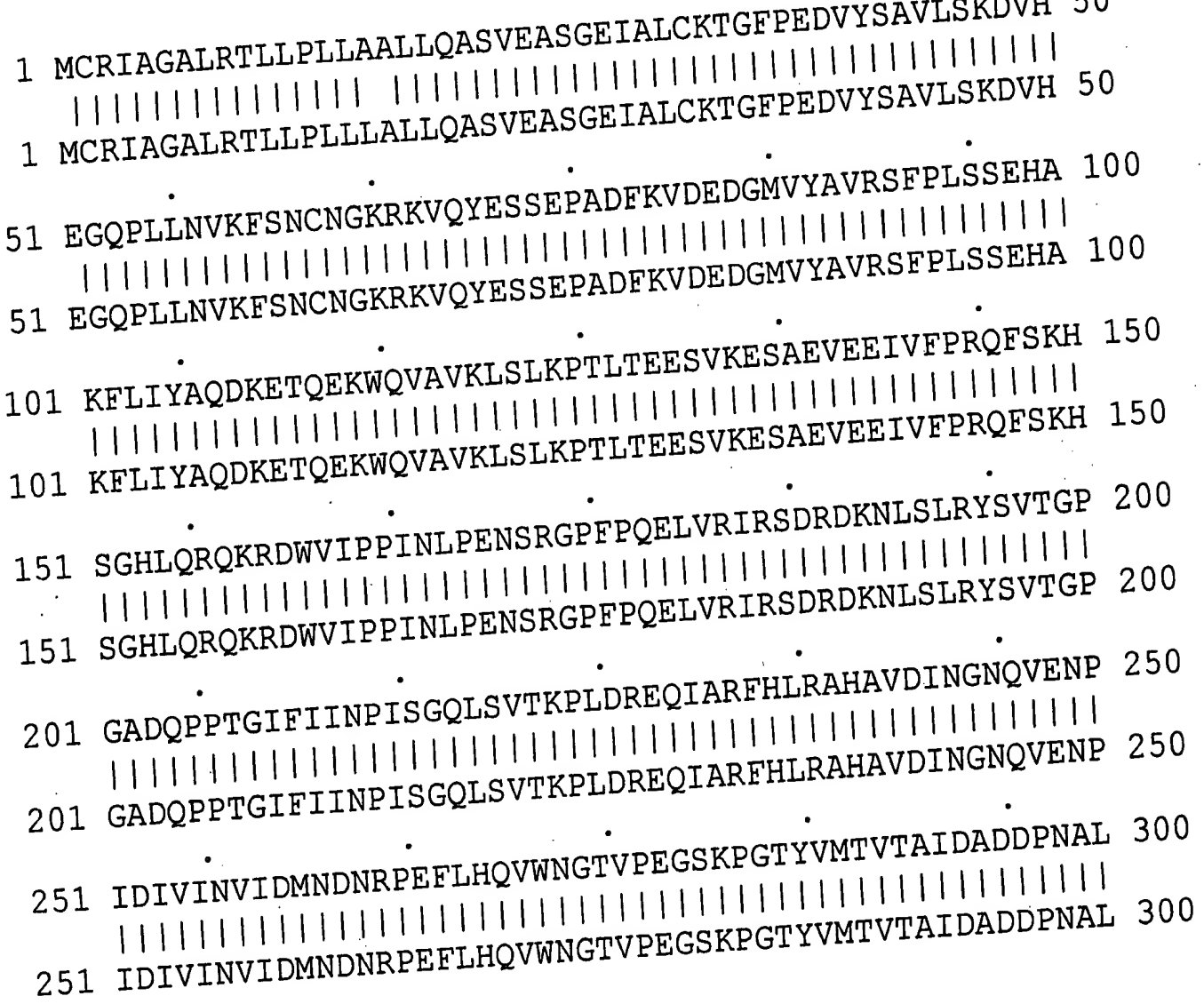
1 MCRIAGALRTLLPLLAALLQASVEASGEIALCKTGFPEDVYSAVLSKDVH 50
1 MCRIAGALRTLLPLLLALLQASVEASGEIALCKTGFPEDVYSAVLSKDVH 50
51 EGQPLLNVKFSNCNGKRKVQYESSEPADFKVDEDGMVYAVRSFPLSSEHA 100
51 EGQPLLNVKFSNCNGKRKVQYESSEPADFKVDEDGMVYAVRSFPLSSEHA 100
101 KFLIYAQDKETQEKWQVAVKLSLKPTLTEESVKESAEVEEIVFPRQFSKH 150
101 KFLIYAQDKETQEKWQVAVKLSLKPTLTEESVKESAEVEEIVFPRQFSKH 150
151 SGHLQRQKRDWVIPPINLPENSRGPFPQELVRIRSDRDKNLSLRYSVTGP 200
151 SGHLQRQKRDWVIPPINLPENSRGPFPQELVRIRSDRDKNLSLRYSVTGP 200
201 GADQPPTGIFIINPISGQLSVTKPLDREQIARFHLRAHAVDINGNQVENP 250
201 GADQPPTGIFIINPISGQLSVTKPLDREQIARFHLRAHAVDINGNQVENP 250
251 IDIVINVIDMNDNRPEFLHQVWNGTVPEGSKPGTYVMTVTAIDADDPNAL 300
251 IDIVINVIDMNDNRPEFLHQVWNGTVPEGSKPGTYVMTVTAIDADDPNAL 300

Fig. 20

```
301 NGMLRYRIVSQAPSTPSPNMFTINNETGDIITVAAGLDREKVQQYTLIIQ 350
    ||||||||||||||||||||||||||||||||||||||||||||||||||
301 NGMLRYRIVSQAPSTPSPNMFTINNETGDIITVAAGLDREKVQQYTLIIQ 350

351 ATDMEGNPTYGLSNTATAVITVTDVNDNPPEFTAMTFYGEVPENRVDIIV 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 ATDMEGNPTYGLSNTATAVITVTDVNDNPPEFTAMTFYGEVPENRVDIIV 400

401 ANLTVTDKDQPHTPAWNAVYRISGGDPTGRFAIQTDPNSNDGLVTVVKPI 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||
401 ANLTVTDKDQPHTPAWNAVYRISGGDPTGRFAIQTDPNSNDGLVTVVKPI 450

451 DFETNRMFVLTVAAENQVPLAKGIQHPPQSTATVSVTVIDVNENPYFAPN 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||
451 DFETNRMFVLTVAAENQVPLAKGIQHPPQSTATVSVTVIDVNENPYFAPN 500

501 PKIIRQEEGLHAGTMLTTFTAQDPDRYMQQNIRYTKLSDPANWLKIDPVN 550
    ||||||||||||||||||||||||||||||||||||||||||||||||||
501 PKIIRQEEGLHAGTMLTTFTAQDPDRYMQQNIRYTKLSDPANWLKIDPVN 550

551 GQITTIAVLDRESPNVKNNIYNATFLASDNGIPPMSGTGTLQIYLLDIND 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||
551 GQITTIAVLDRESPNVKNNIYNATFLASDNGIPPMSGTGTLQIYLLDIND 600
```

Fig. 20(Cont.)

```
601 NAPQVLPQEAETCETPDPNSINITALDYDIDPNAGPFAFDLPLSPVTIKR 650
    ||||||||||||||||||||||||||||||||||||||||||||||||||
601 NAPQVLPQEAETCETPDPNSINITALDYDIDPNAGPFAFDLPLSPVTIKR 650

651 NWTITRLNGDFAQLNLKIKFLEAGIYEVPIIITDSGNPPKSNISILRVKV 700
    ||||||||||||||||||||||||||||||||||||||||||||||||||
651 NWTITRLNGDFAQLNLKIKFLEAGIYEVPIIITDSGNPPKSNISILRVKV 700

701 CQCDSNGDCTDVDRIVGAGLGTGAIIAILLCIIILLILVLMFVVWMKRRD 750
    ||||||||||||||||||||||||||||||||||||||||||||||||||
701 CQCDSNGDCTDVDRIVGAGLGTGAIIAILLCIIILLILVLMFVVWMKRRD 750

751 KERQAKQLLIDPEDDVRDNILKYDEEGGGEEDQDYDLSQLQQPDTVEPDA 800
    ||||||||||||||||||||||||||||||||||||||||||||||||||
751 KERQAKQLLIDPEDDVRDNILKYDEEGGGEEDQDYDLSQLQQPDTVEPDA 800

801 IKPVGIRRMDERPIHAEPQYPVRSAAPHPGDIGDFINE 838
    |||||||||||||||||||||||||||||||||||||
801 IKPVGIRRMDERPIHAEPQYPVRSAAPHPGDIGDFINE 838
```

Fig. 20(Cont.)

```
1 MERVKMINVQRLLEAAEFLERRERECEHGYASSFPSMPSPRLQHSKPPRR 50
  ||||||||||||||||||||||||||||||||||||||||||||||||||
1 MERVKMINVQRLLEAAEFLERRERECEHGYASSFPSMPSPRLQHSKPPRR 50

51 LSRAQKHSSGSSNTSTANRSTHNELEKNR 79
   |||||||||.|||||||||||||||||||
51 LSRAQKHSSGTSNTSTANRSTHNELEKNR 79
```

Fig. 21

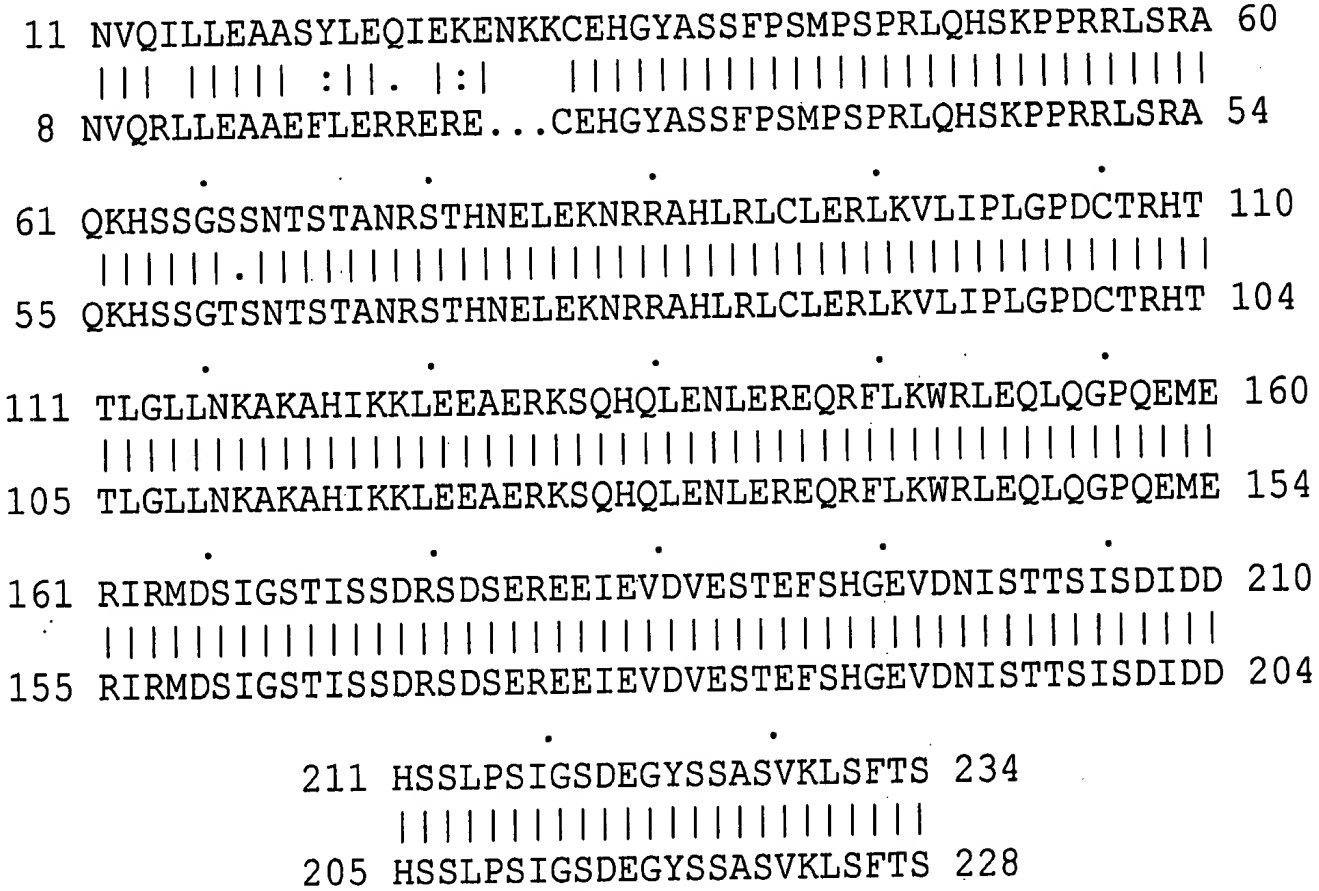
11 NVQILLEAASYLEQIEKENKKCEHGYASSFPSMPSPRLQHSKPPRRLSRA 60
8 NVQRLLEAAEFLERRERE...CEHGYASSFPSMPSPRLQHSKPPRRLSRA 54
61 QKHSSGSSNTSTANRSTHNELEKNRRAHLRLCLERLKVLIPLGPDCTRHT 110
55 QKHSSGTSNTSTANRSTHNELEKNRRAHLRLCLERLKVLIPLGPDCTRHT 104
111 TLGLLNKAKAHIKKLEEAERKSQHQLENLEREQRFLKWRLEQLQGPQEME 160
105 TLGLLNKAKAHIKKLEEAERKSQHQLENLEREQRFLKWRLEQLQGPQEME 154
161 RIRMDSIGSTISSDRSDSEREEIEVDVESTEFSHGEVDNISTTSISDIDD 210
155 RIRMDSIGSTISSDRSDSEREEIEVDVESTEFSHGEVDNISTTSISDIDD 204
211 HSSLPSIGSDEGYSSASVKLSFTS 234
205 HSSLPSIGSDEGYSSASVKLSFTS 228

Fig. 22

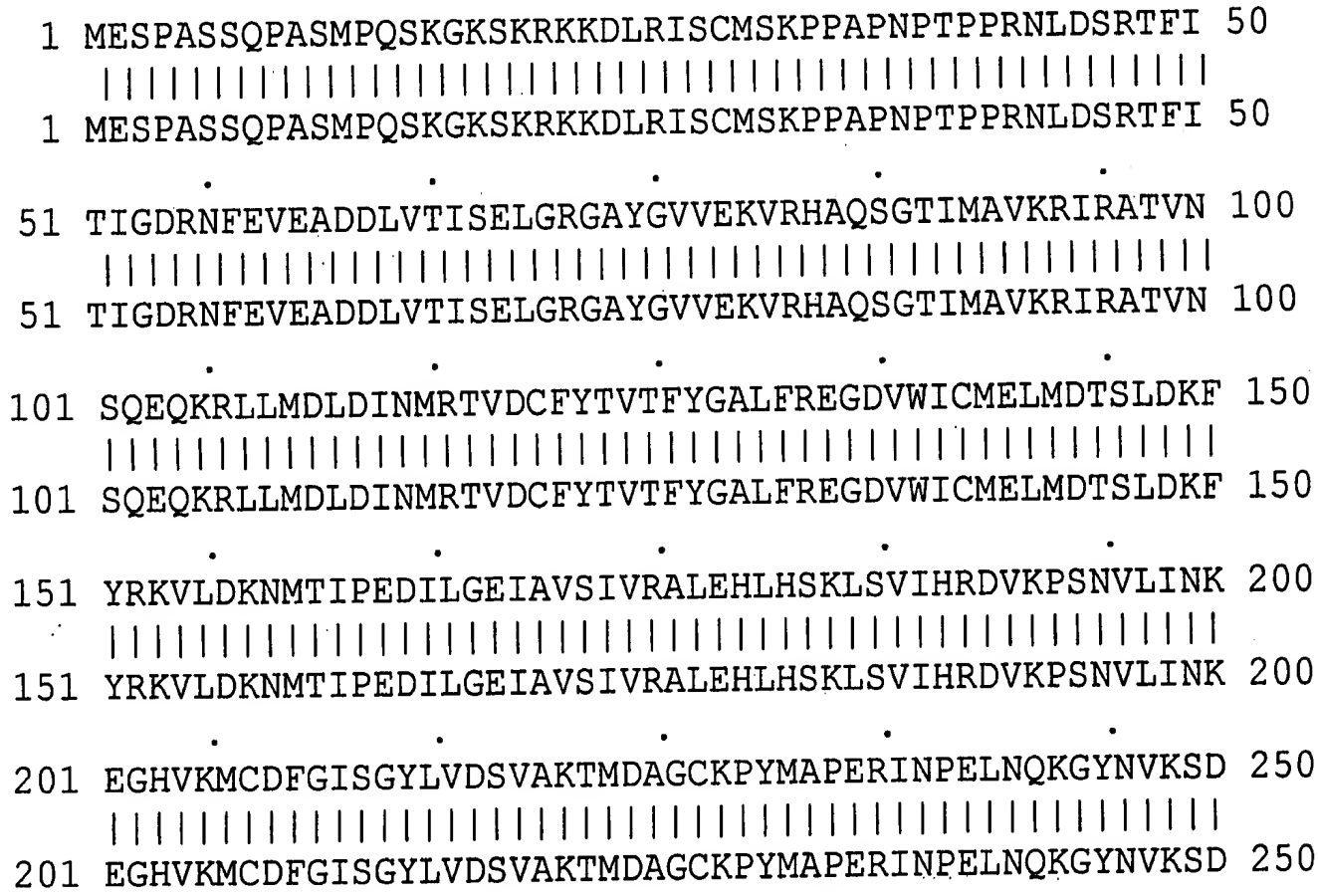
1 MESPASSQPASMPQSKGKSKRKKDLRISCMSKPPAPNPTPPRNLDSRTFI 50
1 MESPASSQPASMPQSKGKSKRKKDLRISCMSKPPAPNPTPPRNLDSRTFI 50
51 TIGDRNFEVEADDLVTISELGRGAYGVVEKVRHAQSGTIMAVKRIRATVN 100
51 TIGDRNFEVEADDLVTISELGRGAYGVVEKVRHAQSGTIMAVKRIRATVN 100
101 SQEQKRLLMDLDINMRTVDCFYTVTFYGALFREGDVWICMELMDTSLDKF 150
101 SQEQKRLLMDLDINMRTVDCFYTVTFYGALFREGDVWICMELMDTSLDKF 150
151 YRKVLDKNMTIPEDILGEIAVSIVRALEHLHSKLSVIHRDVKPSNVLINK 200
151 YRKVLDKNMTIPEDILGEIAVSIVRALEHLHSKLSVIHRDVKPSNVLINK 200
201 EGHVKMCDFGISGYLVDSVAKTMDAGCKPYMAPERINPELNQKGYNVKSD 250
201 EGHVKMCDFGISGYLVDSVAKTMDAGCKPYMAPERINPELNQKGYNVKSD 250

Fig. 23

```
251 VWSLGITMIEMAILRFPYESWGTPFQQLKQVVEEPSPQLPADRFSPEFVD 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
251 VWSLGITMIEMAILRFPYESWGTPFQQLKQVVEEPSPQLPADRFSPEFVD 300

301 FTAQCLRKNPAERMSYLELI 320
    ||||||||||||||||||.
301 FTAQCLRKNPAERMSYLELM 320
```

Fig. 23(Cont.)

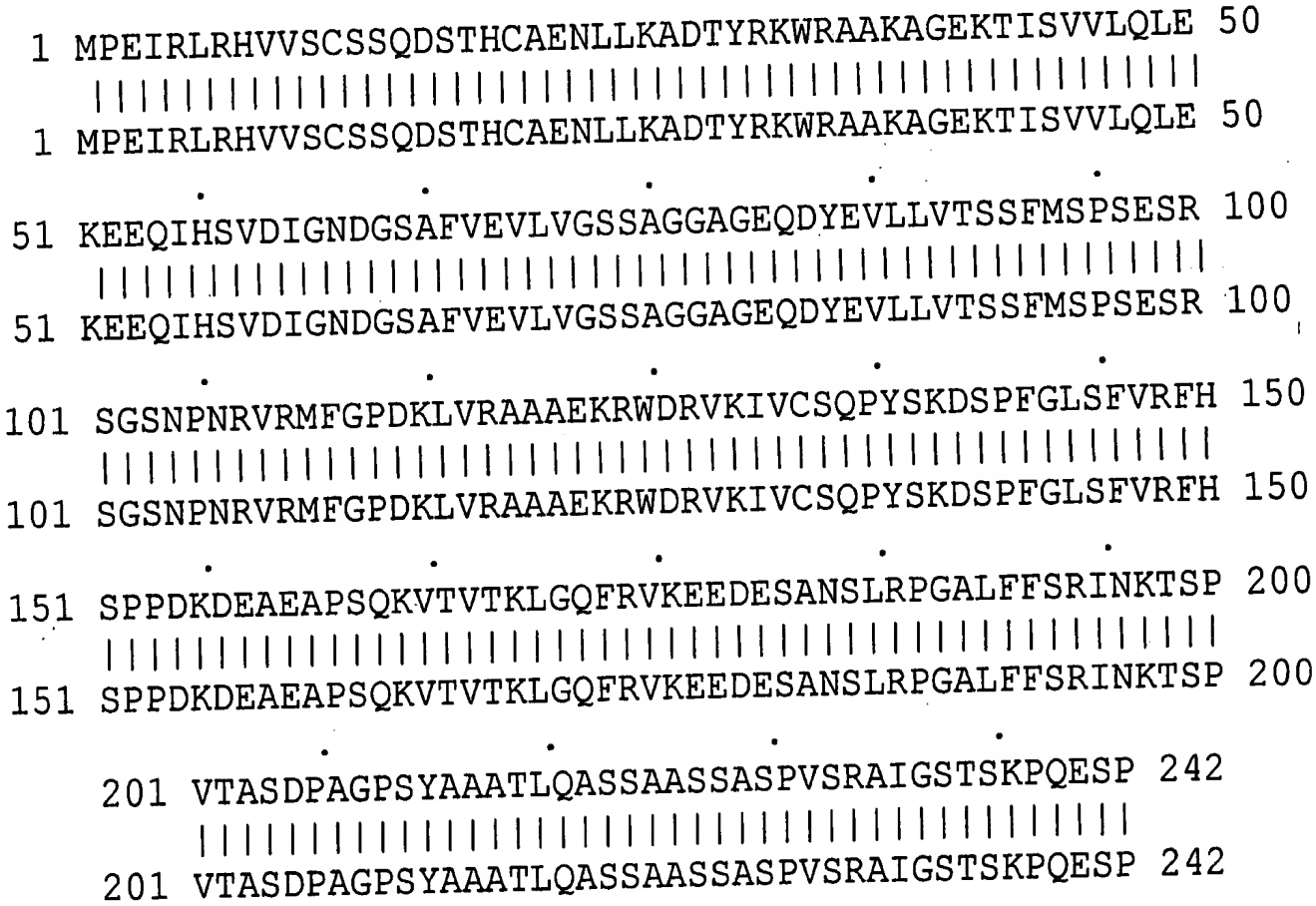
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESP 242
201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESP 242

Fig. 24

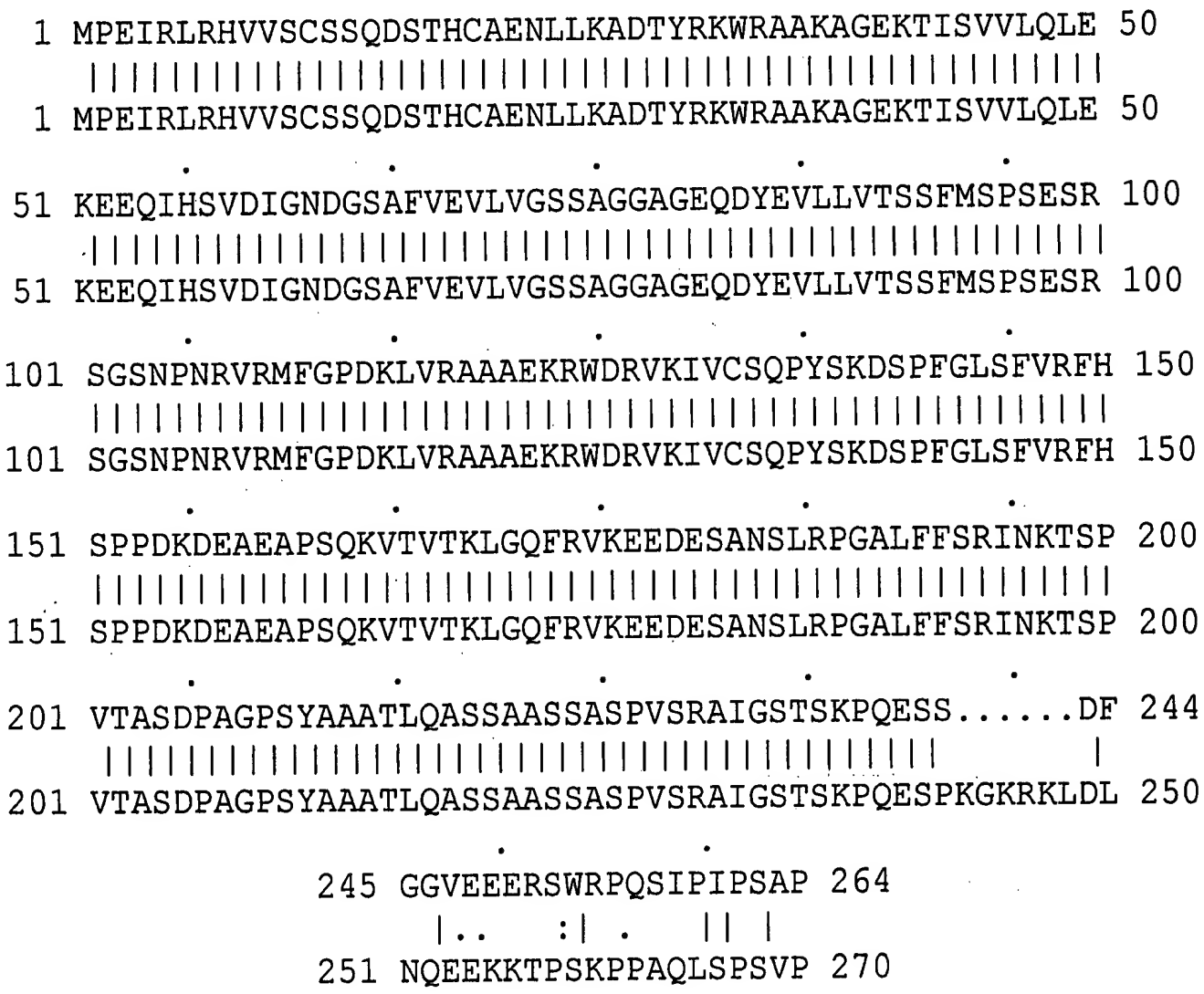
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESS.....DF 244
201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESPKGKRKLDL 250
245 GGVEEERSWRPQSIPIPSAP 264
251 NQEEKKTPSKPPAQLSPSVP 270

Fig. 25

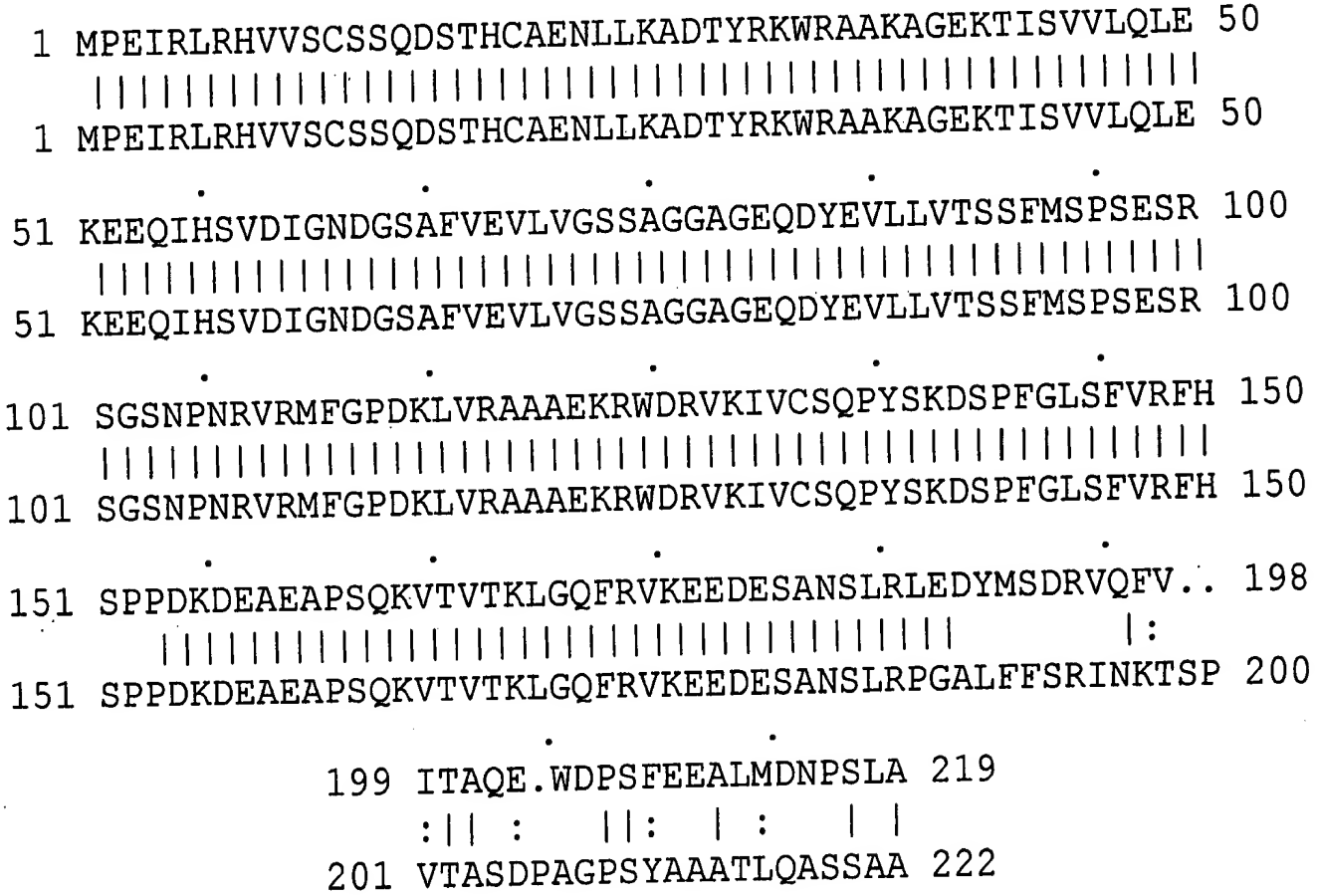
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRLEDYMSDRVQFV.. 198
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
199 ITAQE.WDPSFEEALMDNPSLA 219
201 VTASDPAGPSYAAATLQASSAA 222

Fig. 26

```
  1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50
    ||||||||||||||||||||||||||||||||||||||||||||||||||
  1 MPEIRLRHVVSCSSQDSTHCAENLLKADTYRKWRAAKAGEKTISVVLQLE 50

 51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 51 KEEQIHSVDIGNDGSAFVEVLVGSSAGGAGEQDYEVLLVTSSFMSPSESR 100

101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 SGSNPNRVRMFGPDKLVRAAAEKRWDRVKIVCSQPYSKDSPFGLSFVRFH 150

151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 SPPDKDEAEAPSQKVTVTKLGQFRVKEEDESANSLRPGALFFSRINKTSP 200

201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESPKGKRKLDL 250
    ||||||||||||||||||||||||||||||||||||||||||||||||||
201 VTASDPAGPSYAAATLQASSAASSASPVSRAIGSTSKPQESPKGKRKLDL 250

251 NQEEKKTPSKPPAQLSPSVPKRPKLPAPTRTPATAPVPARAQGAVTGKPR 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||
251 NQEEKKTPSKPPAQLSPSVPKRPKLPAPTRTPATAPVPARAQGAVTGKPR 300
```

Fig. 27

```
301 GEGTEPRRPRAGPEELGKILQGVVVVLSGFQNPFRSELRDKALELGAKYR 350
    ||||||||||||||||||||||||||||||||||||||||||||||||||
301 GEGTEPRRPRAGPEELGKILQGVVVVLSGFQNPFRSELRDKALELGAKYR 350

351 PDWTRDSTHLICAFANTPKYSQVLGLGGRIVRKEWVLDCHRMRRRLPSRR 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 PDWTRDSTHLICAFANTPKYSQVLGLGGRIVRKEWVLDCHRMRRRLPSRR 400

401 YLMAGPGSSSEEDEASHSGGSGDEAPKLPQKQPQTKTKPTQAAGPSSPQK 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||
401 YLMAGPGSSSEEDEASHSGGSGDEAPKLPQKQPQTKTKPTQAAGPSSPQK 450

451 PPTPEETKAASPVLQEDIDIEGVQSEGQDNGAEDSGDTEDELRRVAEQKE 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||
451 PPTPEETKAASPVLQEDIDIEGVQSEGQDNGAEDSGDTEDELRRVAEQKE 500

501 HRLPPGQEENGEDPYAGSTDENTDSEEHQEPPDLPVPELPRFLPGQ 546
    |||||||||||||||||||||||||||||||||| |  |.
501 HRLPPGQEENGEDPYAGSTDENTDSEEHQEPPDLPVPELPDFFQGK 546
```

Fig. 27(Cont.)

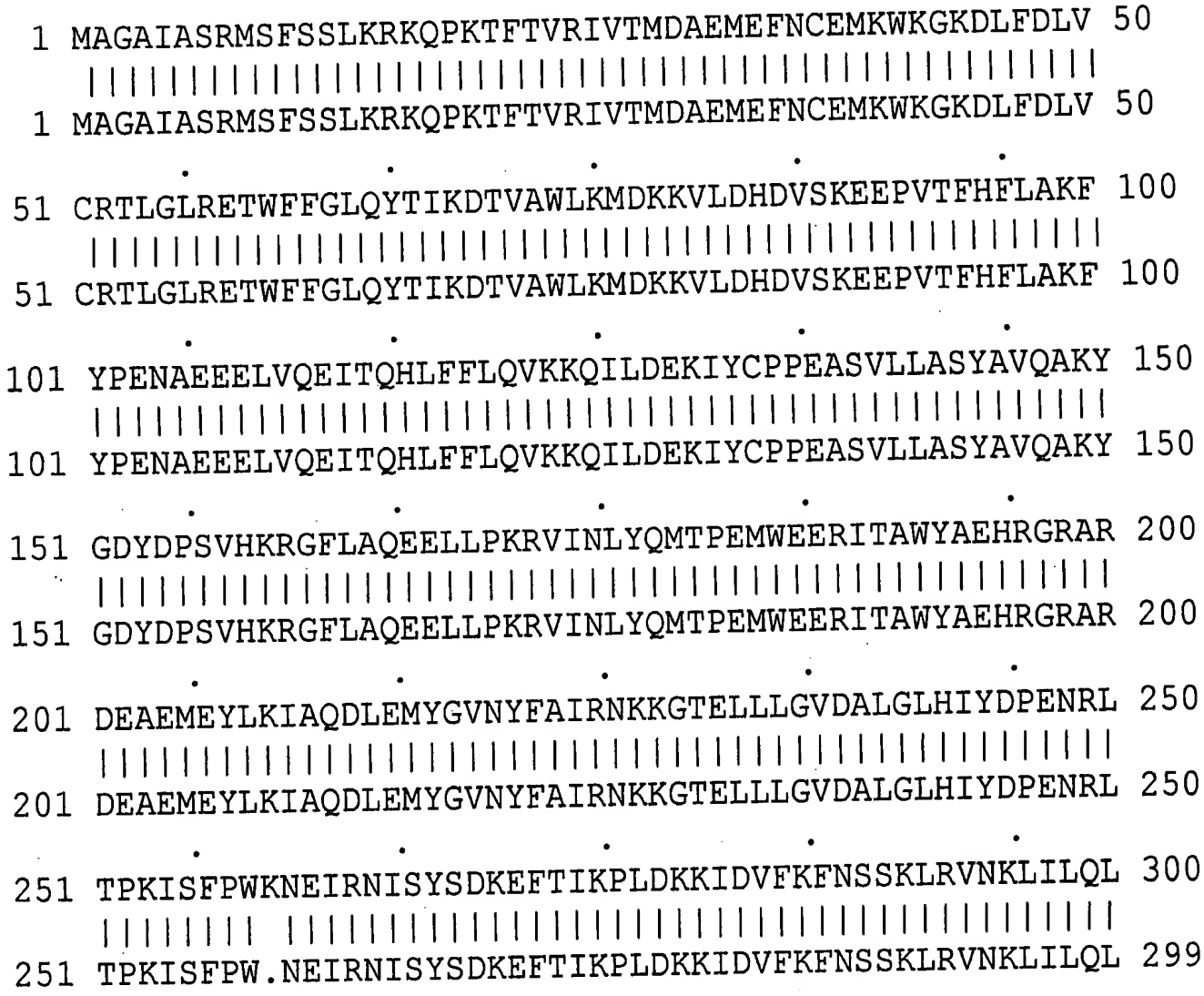
1 MAGAIASRMSFSSLKRKQPKTFTVRIVTMDAEMEFNCEMKWKGKDLFDLV 50
1 MAGAIASRMSFSSLKRKQPKTFTVRIVTMDAEMEFNCEMKWKGKDLFDLV 50
51 CRTLGLRETWFFGLQYTIKDTVAWLKMDKKVLDHDVSKEEPVTFHFLAKF 100
51 CRTLGLRETWFFGLQYTIKDTVAWLKMDKKVLDHDVSKEEPVTFHFLAKF 100
101 YPENAEEELVQEITQHLFFLQVKKQILDEKIYCPPEASVLLASYAVQAKY 150
101 YPENAEEELVQEITQHLFFLQVKKQILDEKIYCPPEASVLLASYAVQAKY 150
151 GDYDPSVHKRGFLAQEELLPKRVINLYQMTPEMWEERITAWYAEHRGRAR 200
151 GDYDPSVHKRGFLAQEELLPKRVINLYQMTPEMWEERITAWYAEHRGRAR 200
201 DEAEMEYLKIAQDLEMYGVNYFAIRNKKGTELLLGVDALGLHIYDPENRL 250
201 DEAEMEYLKIAQDLEMYGVNYFAIRNKKGTELLLGVDALGLHIYDPENRL 250
251 TPKISFPWKNEIRNISYSDKEFTIKPLDKKIDVFKFNSSKLRVNKLILQL 300
251 TPKISFPW.NEIRNISYSDKEFTIKPLDKKIDVFKFNSSKLRVNKLILQL 299

Fig.28

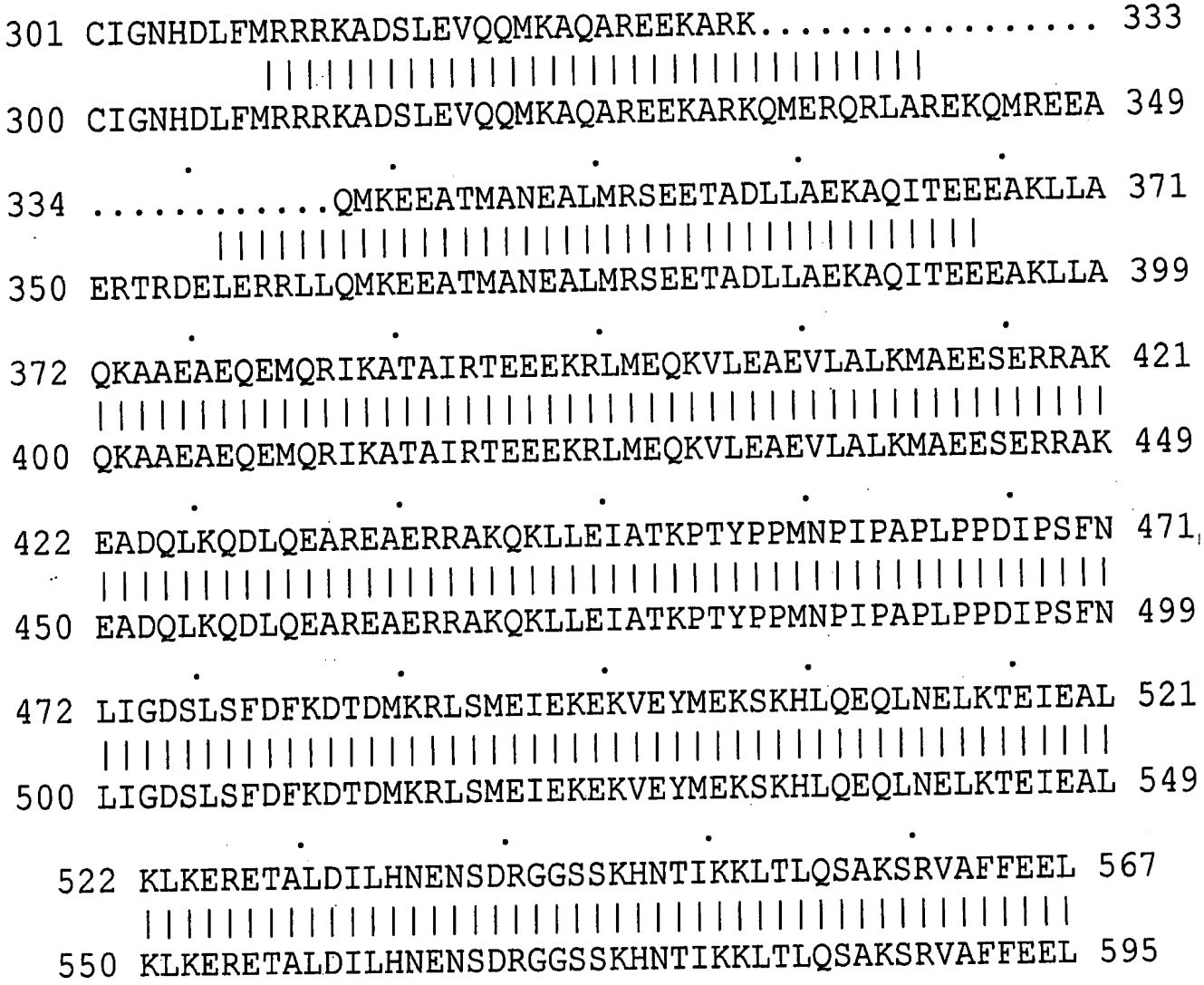
301 CIGNHDLFMRRRKADSLEVQQMKAQAREEKARK..... 333
300 CIGNHDLFMRRRKADSLEVQQMKAQAREEKARKQMERQRLAREKQMREEA 349
334 .....QMKEEATMANEALMRSEETADLLAEKAQITEEEAKLLA 371
350 ERTRDELERRLLQMKEEATMANEALMRSEETADLLAEKAQITEEEAKLLA 399
372 QKAAEAEQEMQRIKATAIRTEEEKRLMEQKVLEAEVLALKMAEESERRAK 421
400 QKAAEAEQEMQRIKATAIRTEEEKRLMEQKVLEAEVLALKMAEESERRAK 449
422 EADQLKQDLQEAREAERRAKQKLLEIATKPTYPPMNPIPAPLPPDIPSFN 471
450 EADQLKQDLQEAREAERRAKQKLLEIATKPTYPPMNPIPAPLPPDIPSFN 499
472 LIGDSLSFDFKDTDMKRLSMEIEKEKVEYMEKSKHLQEQLNELKTEIEAL 521
500 LIGDSLSFDFKDTDMKRLSMEIEKEKVEYMEKSKHLQEQLNELKTEIEAL 549
522 KLKERETALDILHNENSDRGGSSKHNTIKKLTLQSAKSRVAFFEEL 567
550 KLKERETALDILHNENSDRGGSSKHNTIKKLTLQSAKSRVAFFEEL 595

Fig.28(Cont.)

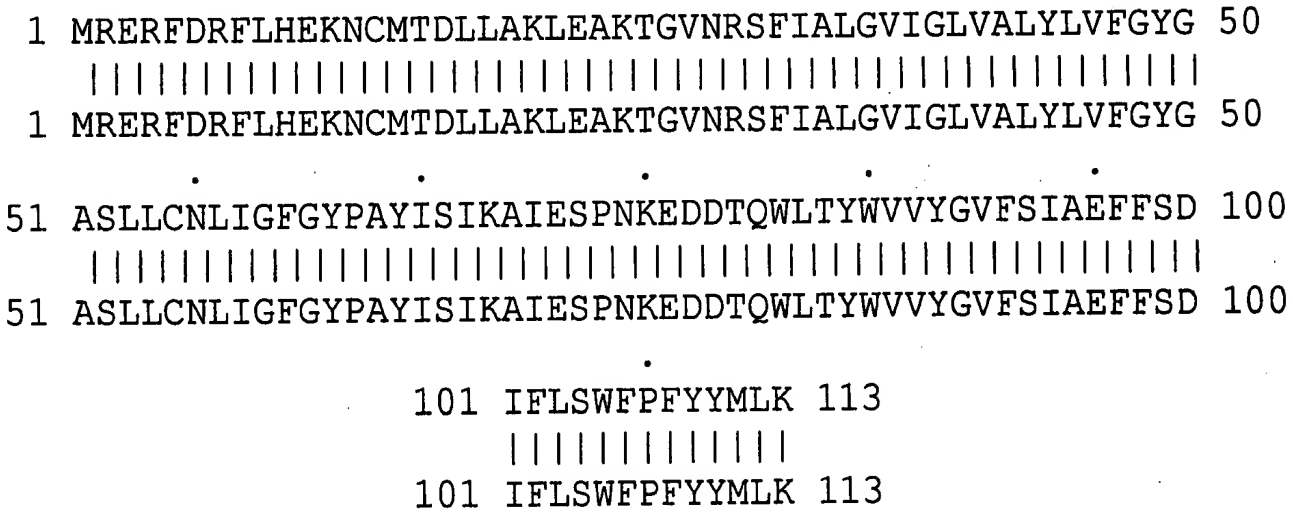
1 MRERFDRFLHEKNCMTDLLAKLEAKTGVNRSFIALGVIGLVALYLVFGYG 50
1 MRERFDRFLHEKNCMTDLLAKLEAKTGVNRSFIALGVIGLVALYLVFGYG 50
51 ASLLCNLIGFGYPAYISIKAIESPNKEDDTQWLTYWVVYGVFSIAEFFSD 100
51 ASLLCNLIGFGYPAYISIKAIESPNKEDDTQWLTYWVVYGVFSIAEFFSD 100
101 IFLSWFPFYYMLK 113
101 IFLSWFPFYYMLK 113

Fig. 29

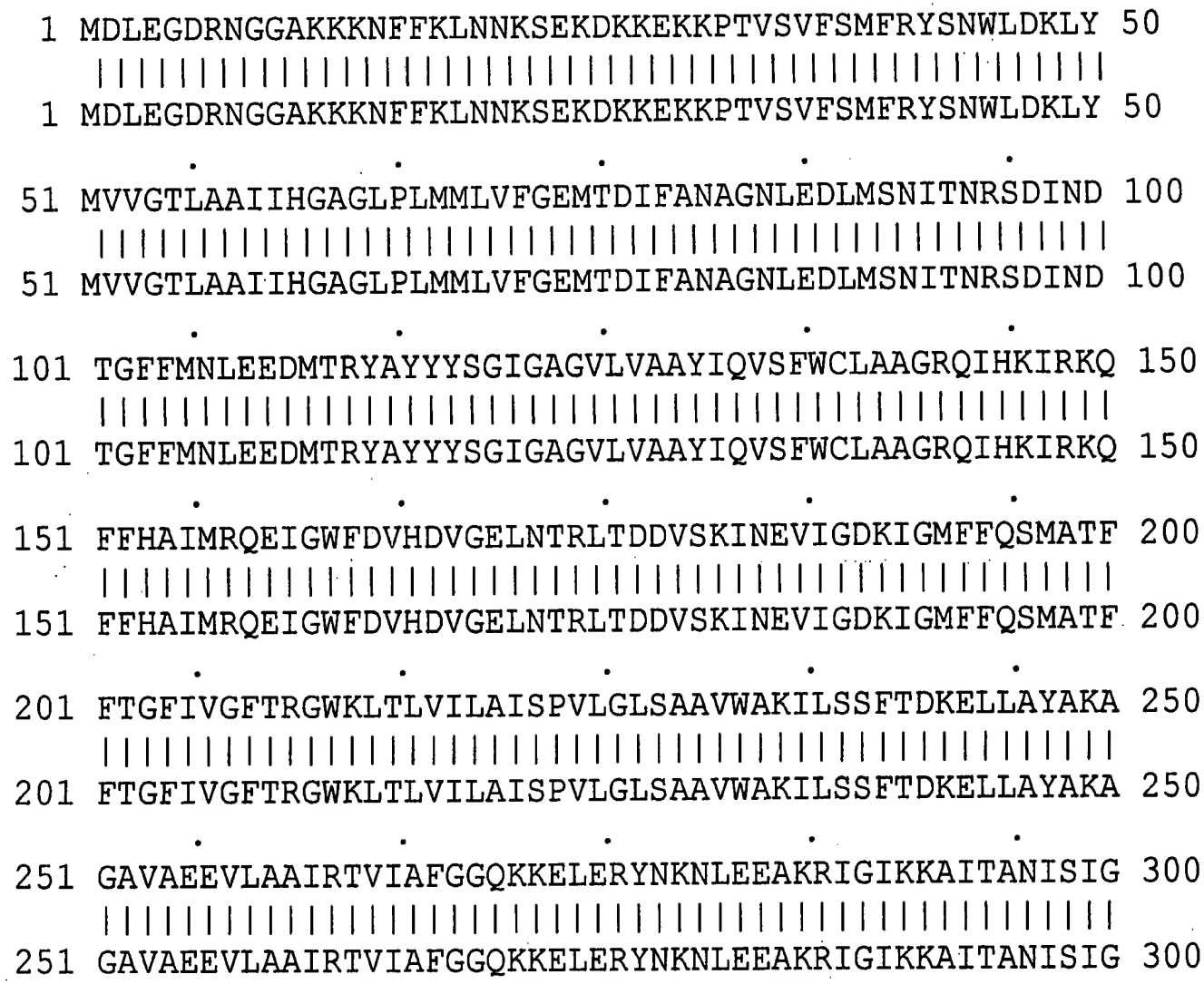
1 MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLY 50
1 MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLY 50
51 MVVGTLAAIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDIND 100
51 MVVGTLAAIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDIND 100
101 TGFFMNLEEDMTRYAYYYSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQ 150
101 TGFFMNLEEDMTRYAYYYSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQ 150
151 FFHAIMRQEIGWFDVHDVGELNTRLTDDVSKINEVIGDKIGMFFQSMATF 200
151 FFHAIMRQEIGWFDVHDVGELNTRLTDDVSKINEVIGDKIGMFFQSMATF 200
201 FTGFIVGFTRGWKLTLVILAISPVLGLSAAVWAKILSSFTDKELLAYAKA 250
201 FTGFIVGFTRGWKLTLVILAISPVLGLSAAVWAKILSSFTDKELLAYAKA 250
251 GAVAEEVLAAIRTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIG 300
251 GAVAEEVLAAIRTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIG 300

Fig. 30

```
301 AAFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASP 350
    ||||||||||||||||||||||||||||||||||||||||||||||||||
301 AAFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASP 350

351 SIEAFANARGAAYEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFS 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 SIEAFANARGAAYEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFS 400

401 YPSRKEVKILKGLNLKVQSGQTVALVGNSGCGKSTTVQLMQRLYDPTEGM 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||
401 YPSRKEVKILKGLNLKVQSGQTVALVGNSGCGKSTTVQLMQRLYDPTEGM 450

451 VSVDGQDIRTINVRFLREIIGVVSQEPVLFATTIAENIRYGRENVTMDEI 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||
451 VSVDGQDIRTINVRFLREIIGVVSQEPVLFATTIAENIRYGRENVTMDEI 500

501 EKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIARALVRNPK 550
    ||||||||||||||||||||||||||||||||||||||||||||||||||
501 EKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIARALVRNPK 550

551 ILLLDEATSALDTESEAVVQVALDKARKGRTTIVIAHRLSTVRNADVIAG 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||
551 ILLLDEATSALDTESEAVVQVALDKARKGRTTIVIAHRLSTVRNADVIAG 600
```

Fig. 30(Cont.)

```
601 FDDGVIVEKGNHDELMKEKGIYFKLVTMQTAGNEVELENAADESKSEIDA 650
    ||||||||||||||||||||||||||||||||||||||||||||||||||
601 FDDGVIVEKGNHDELMKEKGIYFKLVTMQTAGNEVELENAADESKSEIDA 650

651 LEMSSNDSRSSLIRKRSTRRSVRGSQAQDRKLSTKEALDESIPPVSFWRI 700
    ||||||||||||||||||||||||||||||||||||||||||||||||||
651 LEMSSNDSRSSLIRKRSTRRSVRGSQAQDRKLSTKEALDESIPPVSFWRI 700

701 MKLNLTEWPYFVVGVFCAIINGGLQPAFAIIFSKIIGVFTRIDDPETKRQ 750
    ||||||||||||||||||||||||||||||||||||||||||||||||||
701 MKLNLTEWPYFVVGVFCAIINGGLQPAFAIIFSKIIGVFTRIDDPETKRQ 750

751 NSNLFSLLFLALGIISFITFFLQGFTFGKAGEILTKRLRYMVFRSMLRQD 800
    ||||||||||||||||||||||||||||||||||||||||||||||||||
751 NSNLFSLLFLALGIISFITFFLQGFTFGKAGEILTKRLRYMVFRSMLRQD 800

801 VSWFDDPKNTTGALTTRLANDAAQVKGAIGSRLAVITQNIANLGTGIIIS 850
    ||||||||||||||||||||||||||||||||||||||||||||||||||
801 VSWFDDPKNTTGALTTRLANDAAQVKGAIGSRLAVITQNIANLGTGIIIS 850

851 FIYGWQLTLLLLAIVPIIAIAGVVEMKMLSGQALKDKKELEGAGKIATEA 900
    ||||||||||||||||||||||||||||||||||||||||||||||||||
851 FIYGWQLTLLLLAIVPIIAIAGVVEMKMLSGQALKDKKELEGAGKIATEA 900
```

Fig. 30(Cont.)

```
 901 IENFRTVVSLTQEQKFEHMYAQSLQVPYRNSLRKAHIFGITFSFTQAMMY 950
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 901 IENFRTVVSLTQEQKFEHMYAQSLQVPYRNSLRKAHIFGITFSFTQAMMY 950

 951 FSYAGCFRFGAYLVAHKLMSFEDVLLVFSAVVFGAMAVGQVSSFAPDYAK 1000
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 951 FSYAGCFRFGAYLVAHKLMSFEDVLLVFSAVVFGAMAVGQVSSFAPDYAK 1000

1001 AKISAAHIIMIIEKTPLIDSYSTEGLMPNTLEGNVTFGEVVFNYPTRPDI 1050
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1001 AKISAAHIIMIIEKTPLIDSYSTEGLMPNTLEGNVTFGEVVFNYPTRPDI 1050

1051 PVLQGLSLEVKKGQTLALVGSSGCGKSTVVQLLERFYDPLAGKVLLDGKE 1100
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1051 PVLQGLSLEVKKGQTLALVGSSGCGKSTVVQLLERFYDPLAGKVLLDGKE 1100

1101 IKRLNVQWLRAHLGIVSQEPILFDCSIAENIAYGDNSRVVSQEEIVRAAK 1150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1101 IKRLNVQWLRAHLGIVSQEPILFDCSIAENIAYGDNSRVVSQEEIVRAAK 1150

1151 EANIHAFIESLPNKYSTKVGDKGTQLSGGQKQRIAIARALVRQPHILLLD 1200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1151 EANIHAFIESLPNKYSTKVGDKGTQLSGGQKQRIAIARALVRQPHILLLD 1200
```

Fig. 30(Cont.)

```
1201 EATSALDTESEKVVQEALDKAREGRTCIVIAHRLSTIQNADLIVVFQNGR 1250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
1201 EATSALDTESEKVVQEALDKAREGRTCIVIAHRLSTIQNADLIVVFQNGR 1250

1251 VKEHGTHQQLLAQKGIYFSMVSVQAGT 1277
     ||||||||||||||||||||||||||||
1251 VKEHGTHQQLLAQKGIYFSMVSVQAGT 1277
```

Fig. 30(Cont.)

```
  1 MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLY  50
    ||||||||||||||||||||||||||||||||||||||||||||||||||
  1 MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLY  50

 51 MVVGTLAAIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDIND 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 51 MVVGTLAAIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDIND 100

101 TGFFMNLEEDMTRYAYYYSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQ 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 TGFFMNLEEDMTRYAYYYSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQ 150

151 FFHAIMRQEIGWFDVHDVGELNTRLTDDVSKINEGIGDKIGMFFQSMATF 200
    |||||||||||||||||||||||||||||||| ||||||||||||||||
151 FFHAIMRQEIGWFDVHDVGELNTRLTDDVSKINEVIGDKIGMFFQSMATF 200

201 FTGFIVGFTRGWKLTLVILAISPVLGLSAAVWAKILSSFTDKELLAYAKA 250
    ||||||||||||||||||||||||||||||||||||||||||||||||||
201 FTGFIVGFTRGWKLTLVILAISPVLGLSAAVWAKILSSFTDKELLAYAKA 250

251 GAVAEEVLAAIRTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIG 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||
251 GAVAEEVLAAIRTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIG 300
```

Fig. 31

```
301 AAFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASP 350
    ||||||||||||||||||||||||||||||||||||||||||||||||||
301 AAFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASP 350

351 SIEAFANARGAAYEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFS 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 SIEAFANARGAAYEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFS 400

401 YPSRKEVKILKGLNLKVQSGQTVALVGNSGCGKSTTVQLMQRLYDPTEGM 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||
401 YPSRKEVKILKGLNLKVQSGQTVALVGNSGCGKSTTVQLMQRLYDPTEGM 450

451 VSVDGQDIRTINVRFLREIIGVVSQEPVLFATTIAENIRYGRENVTMDEI 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||
451 VSVDGQDIRTINVRFLREIIGVVSQEPVLFATTIAENIRYGRENVTMDEI 500

501 EKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIARALVRNPK 550
    ||||||||||||||||||||||||||||||||||||||||||||||||||
501 EKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIARALVRNPK 550

551 ILLLDEATSALDTESEAEVQAALDKVSR 578
    |||||||||||||||| || ||||  :
551 ILLLDEATSALDTESEAVVQVALDKARK 578
```

Fig. 31(Cont.)

```
  1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50
    ||||||||||||||||||||||||||||||||||||||||||||||||||
  1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50

 51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100

101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150

151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200

201 GYKENTE 207
    ||||| :
201 GYKENVD 207
```

Fig. 32

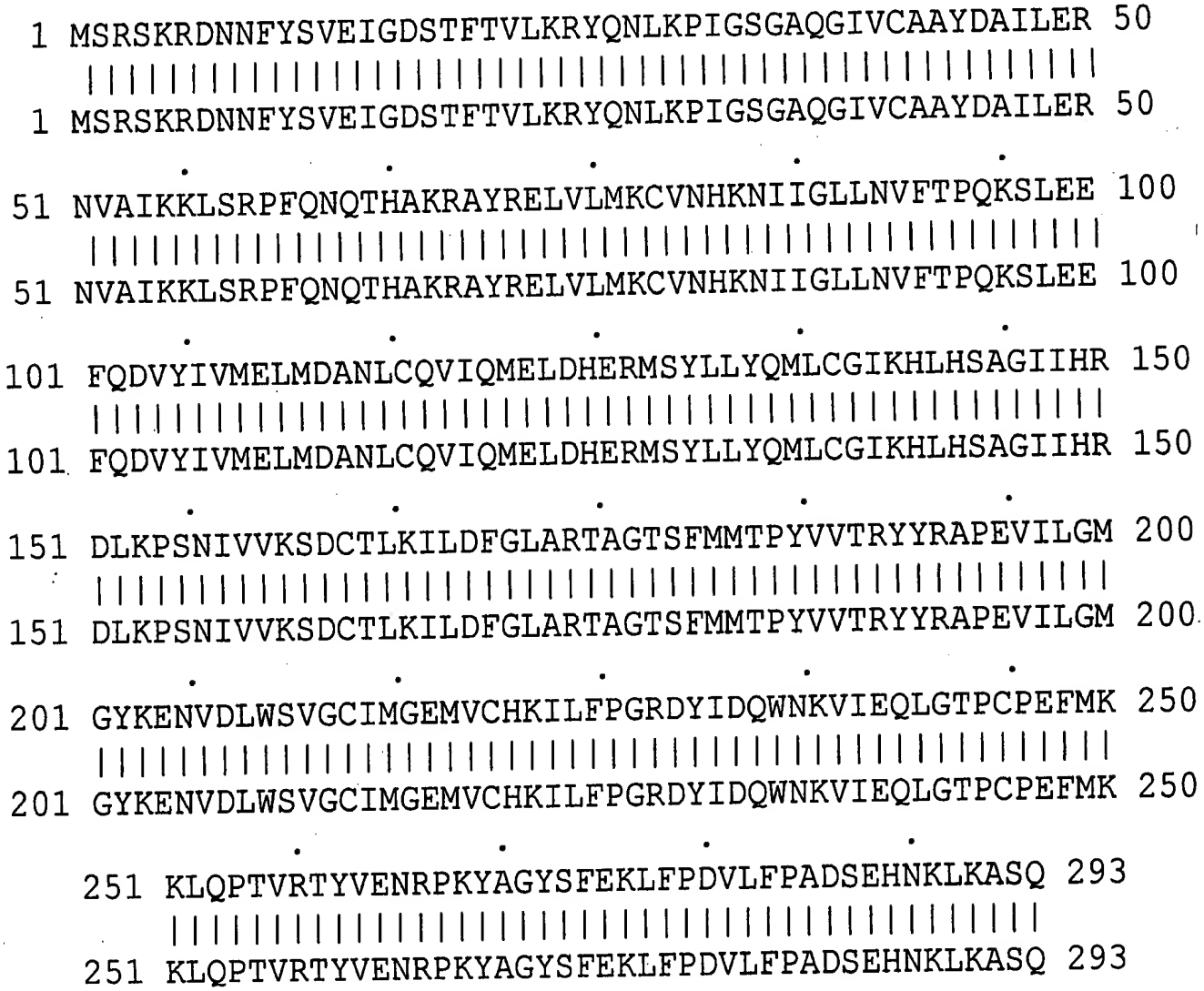
1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50
1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50
51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100
51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100
101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150
101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150
151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200
151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200
201 GYKENVDLWSVGCIMGEMVCHKILFPGRDYIDQWNKVIEQLGTPCPEFMK 250
201 GYKENVDLWSVGCIMGEMVCHKILFPGRDYIDQWNKVIEQLGTPCPEFMK 250
251 KLQPTVRTYVENRPKYAGYSFEKLFPDVLFPADSEHNKLKASQ 293
251 KLQPTVRTYVENRPKYAGYSFEKLFPDVLFPADSEHNKLKASQ 293

Fig. 33

```
  1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50
    ||||||||||||||||||||||||||||||||||||||||||||||||||
  1 MSRSKRDNNFYSVEIGDSTFTVLKRYQNLKPIGSGAQGIVCAAYDAILER 50

 51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 51 NVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIIGLLNVFTPQKSLEE 100

101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 FQDVYIVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHR 150

151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 DLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGM 200

201 GYKENVDLWSVGCIMGEMVCHKILFPGRDYIDQWNKVIEQLGTPCPEFMK 250
    ||||||||||||||||||||||||||||||||||||||||||||||||||
201 GYKENVDLWSVGCIMGEMVCHKILFPGRDYIDQWNKVIEQLGTPCPEFMK 250
```

Fig. 34

```
251 KLQPTVRTYVENRPKYAGYSFEKLFPDVLFPADSEHNKLKASQARDLLSK 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||||
251 KLQPTVRTYVENRPKYAGYSFEKLFPDVLFPADSEHNKLKASQARDLLSK 300

301 MLVIDASKRISVDEALQHPYINVWYDPSEAEARSCKL 337
    |||||||||||||||||||||||||||||||||||  |:
301 MLVIDASKRISVDEALQHPYINVWYDPSEAEAPPPKI 337
```

Fig. 34(Cont.)

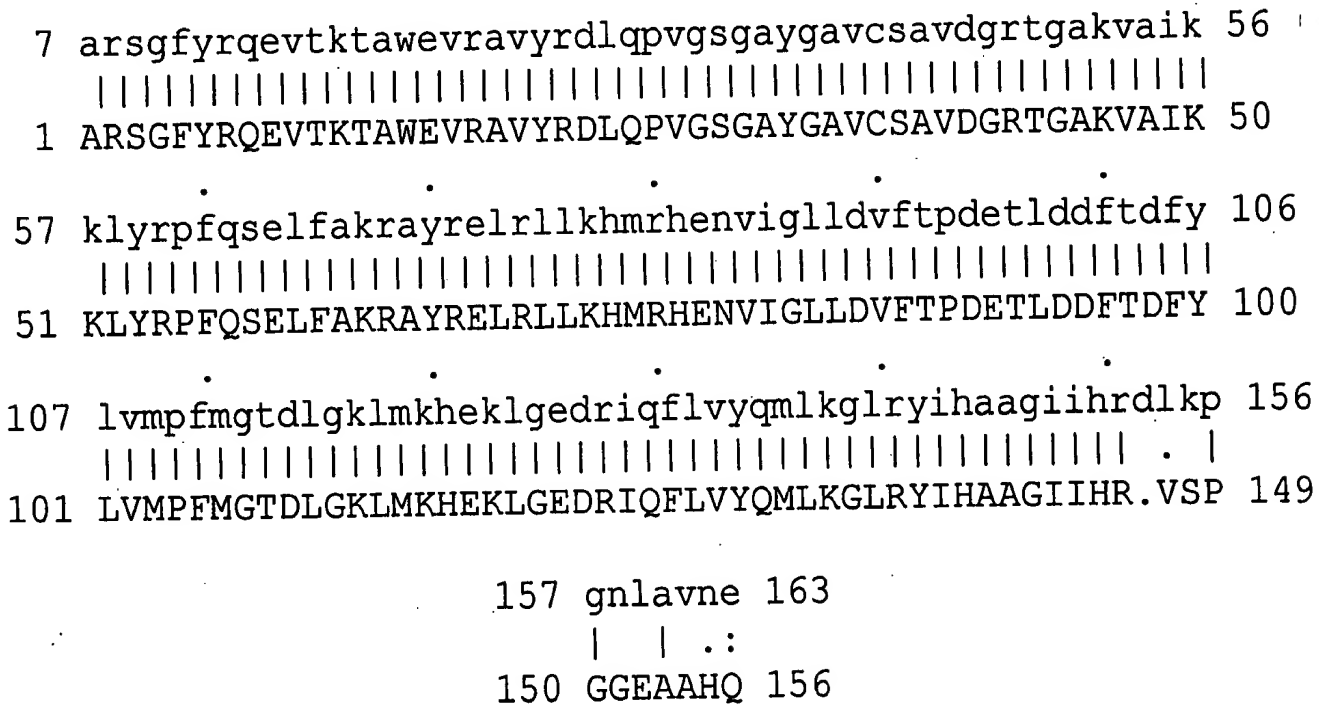
7 arsgfyrqevtktawevravyrdlqpvgsgaygavcsavdgrtgakvaik 56
1 ARSGFYRQEVTKTAWEVRAVYRDLQPVGSGAYGAVCSAVDGRTGAKVAIK 50
57 klyrpfqselfakrayrelrllkhmrhenviglldvftpdetlddftdfy 106
51 KLYRPFQSELFAKRAYRELRLLKHMRHENVIGLLDVFTPDETLDDFTDFY 100
107 lvmpfmgtdlgklmkheklgedriqflvyqmlkglryihaagiihrdlkp 156
101 LVMPFMGTDLGKLMKHEKLGEDRIQFLVYQMLKGLRYIHAAGIIHR.VSP 149
157 gnlavne 163
150 GGEAAHQ 156

Fig. 35

```
  1 MSPFLRIGLSNFDCGSCQSCQGEAVNPYCAVLVKEYVESENGQMYIQKKP 50
    ||||||||||||||||||||||||||||||||||||||||||||||||||
  1 MSPFLRIGLSNFDCGSCQSCQGEAVNPYCAVLVKEYVESENGQMYIQKKP 50

 51 TMYPPWDSTFDAHINKGRVMQIIVKGKNVDLISETTVELYSLAERCRKNN 100
    ||||||||||||||||||||||||||||||||||||||||||||||||||
 51 TMYPPWDSTFDAHINKGRVMQIIVKGKNVDLISETTVELYSLAERCRKNN 100

101 GKTEIWLELKPQGRMLMNARYFLEMSDTKDMNEFETEGFFALHQRRGAIK 150
    ||||||||||||||||||||||||||||||||||||||||||||||||||
101 GKTEIWLELKPQGRMLMNARYFLEMSDTKDMNEFETEGFFALHQRRGAIK 150

151 QAKVHHVKCHEFTATFFPQPTFCSVCHEFVWGLNKQGYQCRQCNAAIHKK 200
    ||||||||||||||||||||||||||||||||||||||||||||||||||
151 QAKVHHVKCHEFTATFFPQPTFCSVCHEFVWGLNKQGYQCRQCNAAIHKK 200

201 CIDKVIAKCTGSAINSRETMFHKERFKIDMPHRFKVYNYKSPTFCEHCGT 250
    ||||||||||||||||||||||||||||||||||||||||||||||||||
201 CIDKVIAKCTGSAINSRETMFHKERFKIDMPHRFKVYNYKSPTFCEHCGT 250
```

Fig. 36

```
251 LLWGLARQGLKCDACGMNVHHRCQTKVANLCGINQKLMAEALAMIESTQQ 300
    ||||||||||||||||||||||||||||||||||||||||||||||||||
251 LLWGLARQGLKCDACGMNVHHRCQTKVANLCGINQKLMAEALAMIESTQQ 300

301 ARCLRDTEQIFREGPVEIGLPCSIKNEARPPCLPTPGKREPQGISWESPL 350
    |||||||||||||||||||||||||| ||||||||||||||||||||
301 ARCLRDTEQIFREGPVEIGLPCSIKNEARLPCLPTPGKREPQGISWESPL 350

351 DEVDKMCHLPEPELNKERPSLQIKLKIEDFILHKMLGKGSFGKVFLAEFK 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 DEVDKMCHLPEPELNKERPSLQIKLKIEDFILHKMLGKGSFGKVFLAEFK 400

401 KTNQFFAIKALKKDVVLMDDDVECTMVEKRVLSLAWEHPFLTHMFCTFQT 450
    ||||||||||||||||||||||||||||||||||||||||||||||||||
401 KTNQFFAIKALKKDVVLMDDDVECTMVEKRVLSLAWEHPFLTHMFCTFQT 450

451 KENLFFVMEYLNGGDLMYHIQSCHKFDLSRATFYAAEIILGLQFLHSKGI 500
    ||||||||||||||||||||||||||||||||||||||||||||||||||
451 KENLFFVMEYLNGGDLMYHIQSCHKFDLSRATFYAAEIILGLQFLHSKGI 500
```

Fig. 36 (Cont.)

```
501 VYRDLKLDNILLDKDGHIKIADFGMCKENMLGDAKTNTFCGTPDYIAPEI 550
    ||||||||||||||||||||||||||||||||||||||||||||||||||
501 VYRDLKLDNILLDKDGHIKIADFGMCKENMLGDAKTNTFCGTPDYIAPEI 550

551 LLGQKYNHSVDWWSFGVLLYEMLIGQSPFHGQDEEELFHSIRMDNPFYPR 600
    ||||||||||||||||||||||||||||||||||||||||||||||||||
551 LLGQKYNHSVDWWSFGVLLYEMLIGQSPFHGQDEEELFHSIRMDNPFYPR 600

601 WLEKEAKDLLVK..VRSEAKSVFIR 623
    ||||||||||||  ||   | . :|
601 WLEKEAKDLLVKLFVREPEKRLGVR 625
```

Fig. 36 (Cont.)